Adverse impact of hospitalisation on infant breastfeeding practices: a prospective cohort study.

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1. Declaration

I, Michelle Rina Alisio, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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2. Abstract

Background: In South Africa, the exclusive breastfeeding prevalence at six months is low at 24% and the under-5 mortality rate remains high. Improving breastfeeding rates is the most cost-effective intervention to reduce under-5 mortality and morbidity. Data on the effect of infant hospitalisation on breastfeeding may inform facility-based interventions to protect and support exclusive and prolonged breastfeeding.

Aim: To assess the impact of hospitalisation on breastfeeding and explore reasons for stopping or continuing breastfeeding.

Methods: We conducted a prospective cohort study of infant feeding practices among mother-infant dyads admitted to general paediatric wards at a tertiary children's hospital in Cape Town, South Africa. Medical, demographic and feeding practice data were collected through semi-structured interviews on admission, again during hospitalisation and a third interview was conducted telephonically post discharge. Logistic regression analysis was used to assess factors associated with different feeding practices.

Results: Between January and April 2018, 119 mothers (median age 26 years, IQR 22-32; 28% HIV-positive) were interviewed at admission; 39% (46/119) breastfed exclusively (EBF) and 28 (24%) reported no breastfeeding. Most infants (median age 1.8 months, IQR 1.0-3.2; 34% preterm) were admitted for lower respiratory tract infection (59%) or diarrhoea (14%). EBF at admission was associated with younger infant age (per month increase, aOR 0.18, 95% CI 0.07-0.43); none of the children admitted for diarrhoea had been EBF. A second in-hospital interview occurred at median 4 days (IQR 2-6) after admission. The overall prevalence of any breastfeeding declined from 77% at admission to 61% in-hospital. Risk factors for in-hospital breastfeeding cessation included low birth weight (<2500g; OR 3.81, 95% CI 1.35-10.74) and feeding via either bottle/tube (OR 51.00, 95% CI 6.38-407.71). Maternal expression of breastmilk (vs no expression in-hospital) was protective against in-hospital breastfeeding cessation (OR 0.07, 95% CI 0.01-0.33). Post-discharge telephonic interviews (median 5 months after discharge) were available for 92 mother-infant dyads; 21 infants were ≤ six months of age, of whom 24% (5/21) were still exclusively breastfeeding. Breastfeeding cessation at any time after admission and before post-discharge telephonic interview was associated with maternal HIV infection (OR 2.82, 95% CI 0.84-9.40), full time employment (OR 4.95, 95% CI 1.40-17.46) and preterm birth (OR 3.53, 95% CI 1.27-9.81).

Conclusion: Prevalence of both any and exclusive breastfeeding was low at admission to hospital, and lack of breastfeeding strongly correlated with increased risk of an infectious morbidity diagnosis. In addition, hospitalisation substantially reduced the probability of continued breastfeeding. In-hospital breastfeeding support and facilitation of breastmilk expression while infants are unable to breastfeed should be increased. Implementation research may define effective in-hospital breastfeeding support interventions.

3. Acknowledgements

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4. List of Tables and Figures

5. Abbreviations

ABF	Any breastfeeding
ANC	Antenatal care
ART	Antiretroviral treatment
ARVs	Anti-retrovirals
BF	Breastfeeding or breastfed
BFC	Breastfeeding Counselling
BFH	Baby Friendly Hospital
BFCI	Breastfeeding Community Initiative
BFHI	Baby Friendly Hospital Initiative
BMS	Breastmilk substitute
EBF	Exclusive breastfeeding or exclusively breastfed
EFF	Exclusive formula feeding or exclusively formula fed
EICF	Early introduction of complementary feeds
FTT	Failure to thrive
HCP	Health Care Provider
HCW	Health Care Worker
HEU	HIV-exposed and uninfected
HIV	Human Immunodeficiency Virus
HU	HIV-unexposed
LBW	Low birth weight
LMICs	Low and middle-income countries
LRTI	Lower respiratory tract infection
MBF	Mother-Baby Friendly
MBFI	Mother-Baby Friendly Initiative
MTCT	Mother-to-Child Transmission
NGT	Nasogastric tube
OGT	Orogastric tube
ORT	Oral rehydration therapy
PMTCT	Prevention of Mother to Child Transmission
RCWMCH	Red Cross War Memorial Children's Hospital
SA	South Africa or South African
SADHS	South African Demographic and Health Survey
UCT	University of Cape Town
U5M	Under -5 mortality
U5MR	Under -5 mortality rate
UNICEF	United Nation International Children's Emergency Fund
WC	Western Cape
WHO	World Health Organisation

6. Chapter one: Background and objectives of literature review

Breastfeeding (BF) improves the survival, health and development of all children. [1] In South Africa (SA), diarrhoea and pneumonia are still significant causes of under-5 mortality (U5MR) and HIV is highly prevalent. Promotion of exclusive breastfeeding (EBF) for the first six months of life is reported as the most cost-effective preventative intervention for reducing U5MR in low-income settings.[1,2,3] Despite this knowledge, the SA EBF prevalence in the first six months remains low at 32% and only 24% are EBF in months five and six.[4] The U5MR remains high at an estimated 42 deaths per 1000 live births in 2017. [5]

Multifactorial determinants of breastfeeding require support at many levels. From policy directives to improve monitoring and enforcement of the Regulation R.991 to ensure compliance with the International Code on marketing of Breastmilk Substitutes (BMS); improved implementation of health care services such as the Baby Friendly Hospital Initiative (BFHI) and more regulated protection of breastfeeding in the workplace. [2]

The role of BF in HIV transmission has evolved and significantly affected policy. Frequent changes to Prevention of Mother-to-Child Transmission (PMTCT) guidelines, especially since 2010, and little investment in BF promotion has undermined BF confidence as well as the quality of HCW advice since the accepted approach to support HIV-positive women to BF.[6,7,8]

Evidence on the effect of hospitalisation on BF in SA, in the current context of promoting universal BF by all mothers, regardless of HIV status, is not known. Data on the effect of hospitalisation may inform interventions to improve BF prevalence now that everyone with HIV may access effective antiretroviral therapy (ART).

This study was based at the Red Cross War Memorial Children's Hospital (RCWMCH), a tertiary care paediatric hospital in the Western Cape, SA. This study investigates the BF practices of hospitalised infants and the impact of hospitalisation itself on infant feeding practice.

To inform this research the objectives of this literature review were:

- To determine the impact of hospitalisation on BF in RCWMCH
- To explore infant feeding practices in RCWMCH
- To investigate the determinants of BF in HIV prevalent settings
- To ascertain the impact of HIV on BF practices in SA
- To explore feeding practices for infants admitted to hospital

6.1. Search strategy

The following search strategy was used to inform this literature review:

Strategy: Search engines were used to search for combinations of the listed search terms (below) from inception until October 2018. Relevant articles suggested by search engines were followed up upon. Related links and references in the selected articles were reviewed. Additional articles and guidelines were included which were recommended by either the supervisor or experts in the field.

Search Engines: PubMed, Google Scholar, Science Direct, Medline (University of Cape Town library)

Search Terms:

- Breastfeeding: exclusive breastfeeding, breastfeeding rate, infant feeding practices, infant nutritional physiological phenomena
- Hospitalisation: admission
- Determinants: effect, adverse effect, impact
- Human Immunodeficiency: HIV seropositivity

Exclusion criteria: Studies from high income countries, dyads with extremely low birth weight infants and non-English articles.

Inclusion criteria: Studies from LMICs, preference for SA articles examining BF prevalence, BF determinants, the role of HIV in infant feeding and associations with hospitalisation.

TABLE 1: Summary of included articles of Literature Review

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Ngcwalisa AJ *et al.* 2018 [9] n=10	Teenagers enrolled from both rural and urban KZN. Total of 6 interviews.	Qualitative Longitudinal cohort	High Teenage pregnancy rate in SA. Maternal family are primary source of emotional and financial support in the post-partum period. Poor outcomes for both teenage mother and her baby	Teenage mothers have limited roles in the infant-feeding decision-making process despite knowledge about the benefits of EBF. Infant feeding-decision making was made by elder maternal family members who were not supportive of EBF.	Determinants of infant feeding practices amongst teenage mothers in SA. Missed opportunity in exploring other factors of BF cessation such as the effect of formula marketing Private, safe interview setting in home language. Very small sample size. Not generalizable. No time frame of the 6 interviews or age of infant at time of interview.	Importance of Health Care Worker role in identifying teenage mothers, include key family members as integral part of infant feeding counselling from antenatal care (ANC) throughout infancy.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Chaponda A, Goon D, Hoque M 2017 [10] n=30	Tembisa Hospital (Gauteng) Post-natal HIV-positive mothers	Qualitative, exploratory	Understanding barriers to infant BF Informing public health policy on promotive strategies of BF	Four identified themes: 1.Nurses and relatives significantly influence mothers' feeding choices 2. BF (50%) vs formula (50%) 3.Early initiation of supplementary solids and traditional remedies for 'bowel cleansing'. 4. Inconsistent counselling on infant feeding	Probing/directed questions creating bias Not generalisable Small population size and only HIV positive mothers Quality of counselling was deduced on the outcome of the mothers feeding choice not through structured observation and interviews of counsellors. Short-sighted conclusion – no suggestion of implementing the universal BFH steps	Tembisa Hospital requirement to become a certified Mother-baby Friendly Hospital.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Ruperez M *et al.* 2017 [11] n=1875	Manhica District Hospital, Maputo, Mozambique	Prospective cohort	To help guide clinical care and effective preventative interventions in HEU children	Compared to HIV-unexposed (HU) children, HEU children are at increased risk of hospital admissions [IRR=1.45, 95% CI: (1.15, 1.83); P=0.0015], severe malnutrition [IRR=2.62, 95% CI: (1.45, 4.75); P=0.0014] and death in the first 18 months.	Difference in follow up between both cohorts, with missing data Limited infant feeding practice data on HU cohort and generally as a strategy for improving child survival in HEU children Conclusion did not answer purpose of study	HEU children are a growing population that are at increased risk of malnutrition, hospitalisation and death. Improving EBF practices on HEU group
Kavle JA *et al.* 2017 [12]	48 articles, dated from Jan 2000, from any twenty-five USAID EPCMD countries	Systematic Review	Determine the barriers to EBF in LMICs	Sixteen barriers to EBF found under three domains: 1.Prenatal barriers 2.Barriers at childbirth 3.Barriers in first six months of life	SA studies not included in review Lack of information on country level implementation of the International Code of Marketing of Breast-milk Substitutes.	Cultural and health system barriers need addressing: improving HCW skills and increasing community support for BF. Improved regulations on marketing of breast milk substitutes (BMS), paid maternity leave, BF breaks for working mothers.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Goosen C, McLachlan MH, Schubl C 2014 [3] n=140	Mothers from two low-income communities in the Western Cape	Cross sectional descriptive	Describe infant feeding practices of infants less than six months in low-income settings of the Western Cape	EBF is a rare practice in SA, 6% (n=8) EBF at median infant age 2.0 (mean+/-SD2.0+-1.5). Fluids and foods are introduced as early as 4weeks of age.	Small sample size Detailed information on supplementary feeds and the reconstitution of formula.	SA requires alternative approaches to improve BF initiation rates and improved infant feeding counselling and support if a reduction in U5M is required.
Doherty T *et al.* 2014 [13] n=964	HIV-negative mother-infant pairs subgroup from PROMISE EBF group) from 34 cluster areas of South Africa (Paarl, Umlazi, Rietvlei)	Prospective cohort (from Community-based cluster randomised trial PROMISE EBF)	To investigate factors other than HIV that are responsible for poor child health outcomes	Early cessation of BF before 6 months (HR 2.4; 95% CI 1.2-5.1) and low birth weight (LBW) (HR 2.4; 95% CI 1.3-4.3) were found to increase the risk of a severe event (hospitalisation or death) Maternal completion of high school education was protective against hospitalisation (HR 0.3;95% CI 0.1-0.7)	Study sample purposefully selected Recall bias Inability to distinguish cause of LBW (prematurity vs growth restriction) Large sample Rigorous data	Strengthen primary health care system by including BF promotion, appropriate care for LBW babies, early administration of ORT (oral rehydration therapy).

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Ijumba P *et al.* 2014 [14] n=60	Sub study of randomised control trial Good Start III, Durban, KwaZulu-natal township between 2008 and 2011	Exploratory qualitative	Understanding the value placed on formula feeding and factors driving it by mothers and household members	Thematic analysis: Inadequate involvement of teenage mothers; grandmothers who became replacement mothers; fear of failing to practice EBF for 6 months; partners as formula providers and costly formula milk leading to risky feeding practices.	Small non-randomised sub group sample. Applicable HIV prevalence sample.	Gaps in key health messages. Need for the development of community-orientated programmes with a focus on teenagers and involvement of grandmothers and fathers in infant feeding decision-making.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Rollins N *et al.* 2013 [15] n=2770	pregnant women enrolled in 2 KwaZulu Natal sites.	Non-randomised intervention cohort	Reporting diarrhoeal prevalence and all-cause mortality at 12 months of age according to infant feeding practices among infants born to HIV-infected and uninfected mothers in South Africa.	EBF practices associated with fewer diarrhoeal events compared to mixed or no BF in both HIV-exposed and HU infants. Risk of death by 12months greater in those who were never BF (aHR 3.5, p<0.001) or mixed fed (aHR 2.65, p<0.001) compared to those who were EBF. Increased risk of infant death in those who were EBF for shorter duration compared to EBF for 5-6 months [aHR 2.18 (95% CI, 1.56-3.01); p<0.001] Risk of diarrhoeal prevalence was increased in male infants and those with non-piped water. Increased risk of diarrhoeal morbidity in infants who were BF for 2-4months compared to those who EBF for 5-6months (AHR 1.35 [95% CI, 1.14-1.59])	Large study sample with meaningful comparative group. Novel data including detailed examination of socio-economic and relational factors that may influence diarrhoeal episodes, morbidity and death.	In the context of upscaled ARVs to eliminate new HIV infections among children, there is strong justification to improve HIV-free survival of HIV exposed and non-exposed infants.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Doherty T *et al.* 2012 [16] n=999	Data collected from already enrolled pregnant mothers (from PROMISE EBF group) from 34 cluster areas of South Africa (Paarl, Umlazi, Rietvlei) through interviews	Longitudinal descriptive Sub group analysis of community-based cluster-randomised trial (PROMISE EBF)	To describe determinants of BF cessation by 12 weeks Urgently address these determinants in order to improve the success and public health impact of BF promotion programmes in SA	Predictors of BF cessation by 12 weeks included intention to not or indecision to BF antenatally, breast health problems and mother having her own source of income. Sub-optimal early feeding practices: low initiation of BF within 1 hour and early introduction of other fluids.	Large total study sample but small maternal HIV positive sample size (n=172) Other possible drivers of BF cessation, such as the effect of marketing of formula milk on BF rate was not determined.	Improve antenatal BF counselling particularly for working women together with improved postnatal lactations technique to prevent breast health problems

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Tylleskar, T *et al.* 2011 [17] n=2579	Mother-infant pairs assigned to intervention or control clusters in Burkina Faso, Uganda and South Africa	Multi-centre community-based cluster-randomised behavioural-intervention trial	Assess the effect of breastfeeding counselling by peer counsellors in Africa	SA EBF prevalence on 24hr recall at 12 weeks: 56 (10%) of 535 intervention group and 30 (6%) of 485 control group (1.72, 1.12-2.63). EBF prevalence on 7-day recall: 41 (8%) and 19 (4%) respectively (1.98, 1.30-3.02). EBF prevalence on 24hr recall at 24 weeks: 12 (2%) and two (<1%) (5.70, 1.33-24.26) EBF prevalence on 7-day recall: ten (2%) and one (<1%) (9.83, 1.40-69.14)	The intervention did not affect diarrhoea prevalence. Conclusion answered aims. Reasons explored for the small absolute increase in EBF prevalence in SA.	Low-intensity individual BF peer-counselling is achievable in increasing EBF prevalence.
Nor B *et al.* 2011 [18] n=17	Sub study of PROMISE EBF	Qualitative study	To recognise and address existing socio-cultural barriers to exclusive infant feeding.	Factors promoting BF: absence of infant illness and perceived weight gain. Prohibitive costs of formula milk Factors promoting mixed feeding: Perception of breastmilk inadequacy, stigma associated with not BF and with the use of free formula in HIV-positive mothers, strong cultural beliefs that promote mixed feeding.	Thematic presentations of small sample, single interview method.	Sensitise policy-makers to rethink current approaches of EBF promotion and support: Clarification of promotional messages of EBF particularly the meaning of 'exclusive' for health workers.

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Ladzani R 2011 [6] n=815	HIV-positive mothers from 47 random clinics of Gert Sibande district, Mpumalanga between January to March 2009.	Cross sectional survey study	Assess infant feeding practices and determinants in HIV-positive women	HIV-positive women were more likely to exclusively formula feed (EFF) if older in age, infant delivered at health facility, knowledge of HIV status (compared to unknown status) and being on ART. EBF rate of 35.6% at 4.5-month infant median age.	Causality between comparable variables cannot be excluded. Self-reporting of infant feeding variables. Only HIV-positive mothers included. Only mothers who visited post-natal care services were included.	Identification of gaps in PMTCT knowledge and infant feeding policy. Disseminating uniform messages to pregnant women; nutrition education strategies that aim at fighting the culture of mixed feeding.
Doherty T *et al.* 2006 [19] N=27	HIV positive-women between May 2004 and January 2005 in 3 SA sites.	Longitudinal Qualitative	Determine challenges that HIV-positive women face at different stages of early infant feeding in an era where free formula was provided to those mothers who chose not to BF.	HIV-positive mothers face issues that challenge exclusive infant feeding practices. These include: unsupportive, incorrect and inconsistent HCW advice; family pressure (particularly if there in non-disclosure) and work-related concerns which undermine EBF.	Small qualitative sample, not generalisable	Inconsistent and sometimes incorrect HCW advice (contributes to early cessation of EBF). Formula feeding mothers fear stigmatisation which lead to the introduction of breastmilk (MBF).

Study	Setting and Participants	Study Type	Purpose	Results/ Conclusions	Strengths/ Limitations	Implications
Doherty T 2006 [20] n=40	HIV-positive mothers interviewed from a larger cohort from 3 different SA sites (Rietvlei, Umlazi and Paarl) between February and June 2004	Qualitative study	Explore how HIV has changed the context within how infant feeding decisions are made.	Five key themes characterising infant-feeding experiences: protection of the child; the influence of HCW and significant others on infant feeding; hiding the truth-realities of free formula milk; self-efficacy.	Sample not randomised. Not generalisable to wider populations of HIV-positive mothers. Omission in stressing predominance of MBF within the study sample.	HIV-positive mothers face challenges that have implications for the effectiveness of the PMTCT programme. More research needed for feasible interventions to improve post-partum care and increase exclusive infant feeding practices.

6.2. Summary of Literature review

6.2.1. Infant feeding practices in South Africa

BF practices in SA were suboptimal, even before the emergence of the HIV epidemic. The EBF rate at six months was extremely low at 7% in 1998[21] and had not improved over a 5-year period from 1998 to 8% in 2003.[22]

In 2016, the South African Demographic and Health Survey (SADHS) showed a national EBF prevalence at six months quadruple to 32%.[4] Despite policy changes with key goals to promote BF, legally enforce the Code of Marketing on BMS and stop distribution of free formula milk for HIV-positive women, the U5MR remains high at an estimated 42 deaths per 1000 live births.[5] There has been an increase in the proportion of deaths due to neonatal conditions (30%), a decreased proportion of deaths due to gastroenteritis (10%) and HIV (9%) and an unchanged proportion of deaths due to pneumonia (17%).[23] Constantly changing infant feeding recommendations, especially since 2010, compounds HCW confusion and undermines community and family confidence in BF. On a background of little or no investment in advocacy or media to promote BF (partly due to fears of HIV transmission) as well as the knowledge that lack of BF is associated with infant and child mortality due to infectious diseases, it is remarkable that the 2016 SADHS EBF prevalence at six months has quadrupled to 32% since 2003.

Infant feeding practices in SA are suboptimal. BF initiation rates at 77% are lower than other developing countries (95%).[3] Both Thylleskar *et al.*[17] in a cluster randomised behavioural intervention trial and Goosen [3] in a cross sectional descriptive study demonstrate the low EBF prevalence at or near 3-month infant age; 30 (6%) of 485 (1.72, 1.12-2.63) and 8 (6%) of 140 mothers respectively. Mixed feeding practices are well described in the qualitative studies of Doherty *et al.*[19], Doherty [16] and Goosen.[3] Goosen [3] showed that 75 (85%) of 97 BF mothers introduced non-nutritive liquids before one month of age. Doherty[16] showed that three days after birth, 276 (31%) HIV-negative women and 22 (37%) HIV-positive women had given their infants something other than breastmilk to drink, most commonly sugar water, formula milk and water. There is paucity of longitudinal data on EBF prevalence. Naturally, EBF rates decrease with increasing infant age so the expected EBF rate at or near 6 months is expected to be lower. Alarmingly, Thylleskar *et al.* [17] showed only two (<1%) mothers EBF their infants to six months.

6.2.2. Determinants of breastfeeding in HIV prevalent settings

Unsupported, EBF is challenging for women in full time employment. Doherty *et al's*.[16] longitudinal descriptive subgroup (from PROMISE EBF study) was concerned with factors leading to early cessation of BF amongst women in SA and found a doubled risk of stopping BF in mothers who had any income (aOR 1.9, 95% CI 1.3-2.8). Earlier work by Doherty *et al*.[19] also argued that by 3 months infant age, mothers spend time away from home (either looking for employment or due to full time employment) and did not have the support to sustain EBF, but pointed out that the effects of employment and availability of money and resources such as an electric kettle and a bottle-cleaning brush maintained and supported formula feeding practices which further justified what was suggested by Doherty *et al*'s later study[16].

Mixed messaging leads to mixed feeding. Chaponda [10] demonstrated the significant influence nurses have on feeding choices of new mothers. Ngcwalisa *et al*.[9], Chaponda [10] as well as Doherty *et al*.[16], all in qualitative studies, highlight the inconsistent messaging provided by nursing personnel, and the counselling behaviour of 'telling'; rather than 'allowing' mothers to make an informed decision. As demonstrated in Chaponda [10], mothers who have not been correctly informed or supported, quickly assume that formula is an acceptable feeding option when it is given to other babies in hospital. This suggests the need to increase the number of Baby Friendly Hospitals (BFH) so that consistent infant feeding messaging across hospitals is increased and HCW skills are strengthened to support mothers' feeding choices.

Continued BF support at the household and community level was a central finding in Kavle *et al*'s[12] systematic review and was deemed one of the most powerful interventions to improve BF practices. Ngcwalisa *et al.* [9] and Ijumba *et al*.[14] through qualitative studies demonstrate the influential role that household relatives, in particular grandmothers, have on infant feeding practices. Grandmothers became replacement mothers and partners became formula milk providers which lead to risky feeding practices.[14] Similarly, Ngcwalisa *et al*.[9] showed the limited role teenage mothers have in the infant feeding decision-making process despite their knowledge and intention to EBF.

The Breastfeeding Community Initiative (BFCI), a Kenyan based programme aimed at supporting post-partum mothers discharged back into the community, expands the World Health Organisation (WHO)/United Nations International Children's Emergency Fund (UNICEF) 'tenth step' of the BFHI through community support groups and home visits by community health volunteers throughout the first year of life. Additional work by the large randomised trial PROMISE EBF study in SA demonstrated increased EBF with supportive counselling at household level by community peer supporters compared to those with no peer support (10.5% and 6.2% PR 1.72, 1.12-2.63) [17]; however, the public health benefit was unlikely to be significant at a population level because of a low overall impact of the intervention. PROMISE EBF used individual BF peer-counselling in communities where Kavle *et al*.[12] and Ngcwalisa *et al*.[9] demonstrate the powerful role of household relatives on infant feeding decision making regardless of a mother's intent to EBF. Perhaps the inclusion of household relatives and focus on family BF counselling as opposed to individual BF counselling could have had a potentially larger benefit on the overall impact of the PROMISE EBF intervention.

The perception of insufficient breastmilk has been raised before in the systematic review of Kavle *et al.* [12] and the small qualitative study of Nor *et al.* [18] as a primary reason for BF cessation as well as the early introduction of other foods and liquids. The perception of breastmilk insufficiency is assumed as the cause for an infant's hunger and crying, lack of satiety and lack of sleep making an important incentive and justification for mixed feeding in early infancy.

6.2.3. Breastfeeding and the role of HIV

HIV-positive women face a series of challenges in sustaining EBF. During a time when free commercial formula was provided for HIV-positive mothers who chose not to BF, Doherty T *et al*.[19] through a longitudinal descriptive study demonstrated the challenges these women face at different stages of infant feeding. These included unsupportive, incorrect and inconsistent HCW advice; family pressure to introduce other liquids or solids early

(particularly if there was non-disclosure), the need to return to work and notably for women using formula milk, fear of stigma associated with the collection of free formula milk which lead to the introduction of breastmilk (mixed feeding). Both qualitative cohorts by Doherty [19,20] highlight the high levels of stigma felt by HIV-positive mothers accessing free formula which discouraged them from carrying out their intentions not to mix feed (breastfeed) which ultimately created self-doubt in their infant feeding practices .

Maternal HIV is a significant risk factor for non-exclusive BF practices. None of the nineteen HIV-positive mothers in Goosen's [3] cross sectional descriptive study initiated BF and Doherty *et al.* [16] showed that 99 (58%) of 172 HIV-positive mothers never initiated BF. Despite a small sample group of HIV-positive mothers (n=172/1126), Doherty *et al*.[16] also demonstrated the rarity of EBF practices. Only 2 (18%) who initiated EBF, continued to EBF until 3 months. Ladzani's [6] cross sectional survey (n=815) reported that only 35.6% of HIV-positive mothers were EBF their infants at a median infant age of 4.5 months. The likelihood of EFF, among these HIV-positive mothers (50%), increased with an older age, knowledge of infant HIV status (compared to unknown infant status) and being on ART therapy.

6.2.4. Feeding practices of infants hospitalised for infectious diagnoses

HIV-exposed uninfected (HEU) children are becoming recognised as a growing group with specific health needs. Every year, over 1 million infants are born to HIV-positive women worldwide, the majority of them in low-income countries, and only 210,000 will become HIV-positive.[24] The reason for the vulnerability of HEU children is not entirely clear but Ruperez *et al*. [11] prospective cohort has demonstrated the increased incidence of hospital admissions and severe malnutrition among HEU children compared with HIV unexposed children (HU). Additionally, the large non-randomised intervention cohort by Rollins N *et al*.[15] in the context of effective ART to reduce post-natal HIV transmission, showed the significantly increased risk of diarrhoeal events and death in the first 12 months in infants (both HEU and HU) who were never BF (aHR 3.5, $p<0.001$) or mixed fed (aHR 2.65, $p<0.001$) compared to those who were EBF. A shorter duration of BF compared to EBF for 5-6 months showed an increased risk of infant death.[15] Suboptimal BF, including the early introduction of complementary solids, shorter durations of EBF, regardless of maternal HIV status, are all associated with an adverse infant outcome.

Hospitalisation has the potential to positively influence BF success through contact with HCW who can encourage BF and reinforce breastmilk expression techniques while infants are temporarily unable to BF. Hospitalisation could also have a negative impact on BF because of the stress associated with infant hospitalisation and absence of in-hospital facilities that support BF and breastmilk expression. In addition, HCW disinterest and tendency to prescribe formula milk may negatively affect BF.

6.3. Gaps in the literature

The gaps in the literature have been divided in the following areas:

Infant feeding practices

Few studies have shown that EBF practices in SA are low and short (early cessation before six months). There is paucity of longitudinal data on EBF prevalence in SA and nothing is known about reasons for infant feeding choices once hospitalised as well as how hospitalisation of a sick infant influences maternal feeding choice later once discharged.

Determinants of BF

There are no SA data on the determinants of hospitalisation itself on BF; in the current setting where the BF prevalence is low, the accepted approach to BF regardless of HIV status is supported and antiretrovirals (ARV) are available. The lack of data may indicate that the benefits of BF and BF as a child survival intervention are still under-recognised.

Similar to the developed world, it is well documented that the need to return to work is a major contributing factor to early BF cessation before six months. In SA, mothers stop BF as early as three months in order to look for employment[19], or do not maintain BF because of return to full time employment in order to earn a sustainable income.[16] Mothers do not make infant feeding decisions once discharged home. Instead, they are given inconsistent messaging and counselling from non-facility health staff, community and family members, particularly grandmother's, which are either unsupportive of EBF practices or in conflict with policy (i.e PMTCT).[10]

Feeding practices of infants hospitalised for infectious causes

EBF is associated with fewer diarrhoeal events compared to MBF or no BF in both HEU and HU infants.[15] The shortage of current studies may indicate that the causes and associations of hospitalised infants to a tertiary paediatric hospital (a severe event) are not prioritised as important indicators of child health and child survival.

Need for further research

In Cape Town specifically (and in developing countries in general) there is little knowledge about the potentially adverse effects of infant hospitalisation on successful BF where HIV is prevalent. This represents an overlooked opportunity to identify determinants of unacceptably low EBF prevalence at six months, which in turn may make achieving the World Health Assembly Targets by 2025 unreachable. This may have devastating consequences on child health and U5M. There is an urgent need to investigate the potentially adverse impact of hospitalisation on BF success and reasons for infant feeding choice. There is also an urgent need to create awareness of the suboptimal infant feeding practices that undermine the health and survival of SA children.

Contribution of thesis to literature

This study will add information on BF prevalence at presentation to hospital, during hospitalisation and after discharge. In addition, more insight into mothers feeding practices, potential barriers to BF in-hospital and the impact of hospitalisation itself on feeding practices will be investigated. If the findings are significant, both risk and protective factors of hospitalisation on BF success could be determined and add further to the literature. It would be the only SA study that could demonstrate, in detail, what factors determine improved BF practices. This study also helps highlight the need for improved public health approach to urgently address the unacceptably low BF.

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7. Chapter two : Publication-ready Manuscript

7.1. Title Page

Adverse impact of hospitalisation on infant breastfeeding practices: a prospective cohort study.

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Research was performed at the general Paediatric wards, Red Cross War Memorial Children's Hospital, Cape Town, South Africa

Keywords: exclusive breastfeeding, infant feeding, determinants, hospitalisation, human immunodeficiency

7.2. Abstract

Background: In South Africa, the exclusive breastfeeding prevalence at six months is low at 24% and the under-5 mortality rate remains high. Improving breastfeeding rates is the most cost-effective intervention to reduce under 5 mortality and morbidity. Data on the effect of infant hospitalisation on breastfeeding may inform facility-based interventions to protect and support exclusive and prolonged breastfeeding.

Aim: To assess the impact of hospitalisation on breastfeeding and explore reasons for stopping or continuing breastfeeding.

Methods: We conducted a prospective cohort study of infant feeding practices among mother-infant dyads admitted to general paediatric wards at a tertiary children's hospital in Cape Town, South Africa. Medical, demographic and feeding practice data were collected through semi-structured interviews on admission, again during hospitalisation and a third interview was conducted telephonically post discharge. Logistic regression analysis was used to assess factors associated with different feeding practices.

Results: Between January and April 2018, 119 mothers (median age 26 years, IQR 22-32; 28% HIV-positive) were interviewed at admission; 39% (46/119) breastfed exclusively (EBF) and 28 (24%) reported no breastfeeding. Most infants (median age 1.8 months, IQR 1.0-3.2; 34% preterm) were admitted for lower respiratory tract infection (59%) or diarrhoea (14%). EBF at admission was associated with younger infant age (per month increase, aOR 0.18, 95% CI 0.07-0.43); none of the children admitted for diarrhoea had been EBF. A second in-hospital interview occurred at median 4 days (IQR 2-6) after admission. The overall prevalence of any breastfeeding declined from 77% at admission to 61% in-hospital. Risk factors for in-hospital breastfeeding cessation included low birth weight (<2500g; OR 3.81, 95% CI 1.35-10.74) and feeding via either bottle/tube (OR 51.00, 95% CI 6.38-407.71). Maternal expression of breastmilk (vs no expression in-hospital) was protective against in-hospital breastfeeding cessation (OR 0.07, 95% CI 0.01-0.33). Post-discharge telephonic interviews (median 5 months after discharge) were available for 92 mother-infant dyads; 21 infants were ≤ six months of age, of whom 24% (5/21) were still exclusively breastfeeding. Breastfeeding cessation at any time after admission and before post-discharge telephonic interview was associated with maternal HIV infection (OR 2.82, 95% CI 0.84-9.40), full time employment (OR 4.95, 95% CI 1.40-17.46) and preterm birth (OR 3.53, 95% CI 1.27-9.81).

Conclusion: Prevalence of both any and exclusive breastfeeding was low at admission to hospital, and lack of breastfeeding strongly correlated with increased risk of an infectious morbidity diagnosis. In addition, hospitalisation substantially reduced the probability of continued breastfeeding. In-hospital breastfeeding support, and facilitation of breastmilk expression while infants are unable to breastfeed should be increased. Implementation research may define effective in-hospital breastfeeding support interventions.

7.3. Introduction

Breastfeeding (BF) improves the survival, health and development of all children.[1] Promotion of exclusive breastfeeding (EBF) for the first six months of life is the most cost-effective intervention for reducing under-5 mortality (U5M) in all children in low-income settings. [1,2,3] In South Africa (SA), gastroenteritis and pneumonia are still significant causes of U5M, the proportion of deaths due to neonatal conditions has increased and maternal HIV is highly prevalent. [23] Despite this knowledge, the SA EBF rate in the first six months remains low at 32% [4] and the U5MR remains high at 42 deaths per 1000 live births. [5]

The Baby Friendly Hospital Initiative (BFHI) is a proven intervention that has a positive impact on BF outcomes. [25] Since 2011, it was implemented under a different name - the Mother-Baby Friendly Initiative (MBFI) which added three additional steps: Compliance to the International Code of Marketing on Breastmilk Substitutes (BMS), infant feeding in the context of HIV, and promoting mother friendly care. Thirteen steps form a continuum of care that starts antenatally in a facility, and continues after birth in a supportive home and community environment. [26] The number of accredited Mother-Baby Friendly (MBF) facilities nationally reached 75% by 2015. [26] There is varied accreditation progress amongst provinces and despite Western Cape (WC) having a well above national accreditation implementation of 98%, Red Cross War Memorial Children's Hospital (RCWMCH), a tertiary paediatric hospital, is still not an accredited MBF hospital.

In 2001, the SA government introduced the Prevention of Mother-to-Child Transmission (PMTCT) programme, primarily aimed at reducing HIV transmission from mothers living with HIV to their infants. Given the existing knowledge at the time and concerns of vertical transmission, those guidelines recommended BF cessation at 4 months for HIV-positive women. Furthermore, provision of free formula milk was made from public health facilities for HIV-positive women choosing not to BF. [27] Annual PMTCT updates followed until in 2015 free formula milk was eventually restricted to high-risk mother-infant HIV pairs failing second- or third-line anti-retroviral treatment (ART). [28] Frequent PMTCT guideline changes, especially since 2010, and little investment in BF advocacy has undermined BF confidence in mothers as well as the quality of health care worker (HCW) advice.[6-8] HIV-positive mothers face many obstacles at different stages of infant feeding that challenge exclusive infant feeding practices.[19] These include unsupportive, incorrect and inconsistent HCW advice; family pressure (particularly if there is non-disclosure) and work-related concerns which undermine EBF.[19]

Ongoing BF support at household and community level significantly improves BF practices in low- and middle-income countries (LMIC's) [12] but establishing a BF friendly environment in non-birthing health facilities remains a challenge. Hospitalisation for infectious causes is known to be associated with non-exclusive BF practices and shorter BF durations [15] and the use of bottles and nasogastric tube feeding in hospitals decreases the extent and duration of BF. [29]

Additional barriers to BF success in hospitalised infants and the potential impact of hospitalisation itself on BF have not been established. We used longitudinal data from a tertiary paediatric hospital in the WC in 2018 to investigate the potential adverse effects of infant hospitalisation on successful BF.

7.4. Objectives

Hypothesis: Hospitalisation of infants impacts BF in a SA setting where the BF prevalence is unacceptably low.

Primary Objective:

To determine prevalence of EBF in infants younger than six months admitted to RCWMCH at admission, during hospitalisation and post-discharge, at 6 months of age.

Secondary Objectives:

Identify factors associated with EBF at all stages.

7.5 Methods

7.5.1. Study design

We used a prospective cohort design of biological mothers, primary caregivers and their hospitalised infants aged less than six months to the general paediatric wards of a tertiary paediatric hospital.

7.5.2. Setting

Between January and April 2018, we recruited mothers whose infants were hospitalised for general paediatric diagnoses that required longer than seventy-two-hour management to the general paediatric wards of RCWMCH in Cape Town, SA. RCWMCH is a level 3 tertiary paediatric hospital within the Cape Town Metro West geographical service area of the WC. The option of rooming-in (allowed to stay by infant bedside for the duration of hospitalisation) is available for all mothers of infants admitted to the general paediatric wards. Mothers opting to room-in are provided with a sleeper couch beside the infant's bed, free meals and use of shower facilities within the ward. Lodging facilities (outside main hospital but within hospital premises) are available for mothers of infants admitted to the paediatric intensive care unit (PICU). Mothers can continue use of lodging facilities after infants are down referred to the general paediatric wards.

7.5.3. Participants

A convenience sample of biological mothers and primary caregivers, including their hospitalised infants less than six months of age, were selected from the general medical paediatric wards. We were only able to include mothers who were by their infants' bedside and telephonically contactable. All mothers under the age of 18 years assented and their parents or legal guardians consented. One mother refused consent and was therefore not included in the study.

7.5.4. Data Collection

In-hospital interviews were conducted mostly after 17:00 when the likelihood of mother-infant pairs at the hospital bedside was greater. Medical, demographic and feeding data were collected through semi-structured questionnaires on paper at the time of the interview and later collated onto an Excel spreadsheet. Current feeding practice data were reported. The age when the first supplement (liquids including water and/or early complementary feeds) of any kind were introduced provided the duration of exclusive breastfeeding. Four feeding groups were used: exclusive breastfeeding (EBF), mixed breastfeeding (MBF, further divided into partial and predominant), no breastfeeding (no BF) and any BF. Any BF and MBF groups included those mothers who initiated breastfeeding and added other liquids/early complementary feeds at any time prior to the first interview. The main interview question was " What are you feeding your baby? Regardless of maternal response to the initial question the interviewer would always include... "Are you feeding your baby anything else and if so, how old was your baby when you introduced it?" The interviewer avoided the use of the term “exclusive breastfeeding”, and rather focused on outlining exactly what nutritional substances the mother provided. The first interview occurred close to or at the time of infant hospitalisation in a private counselling room or other private room within the same ward but away from the infant’s bedside. A second interview was performed prior to discharge (or occasionally performed as part of the first interview) using the infant’s in-hospital prescription and feeding charts. Interviews were conducted by an English-speaking paediatric registrar in training and a dietician. A translator or HCW assisted when translations were required, translating verbally during the interview. Limited study resources did not allow for formal written translations of the questionnaire.

Post-discharge telephonic follow-up interviews were performed from a designated hospital land line, by the paediatric registrar. These interviews occurred over one month between July and August 2018. One or both telephone numbers provided by the participants were utilised and no mothers contacted were unable to interview because of language. A participant was deemed lost to follow up if both numbers were unsuccessful in reaching the participant after multiple attempts. A translator was not available for the post-discharge follow-up period.

7.5.5. Data Analysis for qualitative data

Open-ended questions were used to explore maternal reasons for feeding choice and experience of in-hospital breastmilk expression. All descriptive data was transcribed verbatim. Data analysis was conducted manually (no software program was used) and followed a thematic content method where recurrent themes were identified. Texts of an interview that covered similar issues or experiences were marked and linked to texts of other interviews.

7.5.5. Variables for quantitative analysis

Differences in baseline characteristics were evaluated between BF and non-BF participants. Baseline infant characteristics included in the analysis were gestational age, birthweight, nutrition (weight and length z-scores) and HIV status. Baseline maternal characteristics included age, socio-economic situation, level of education, employment, HIV and marital status, water source, sanitation and electricity availability. Variables assessed in the regression analysis included maternal age and HIV status, level of education, employment, household amenity availability, relationship with infant’s father, infant feeding practice prior

to hospitalisation, preterm birth, low birth weight, infant gender, primary diagnosis, in-hospital maternal breastmilk expression, in-hospital bottle and/or nasogastric tube feeding.

7.5.6. Bias

Interviewer bias was partially addressed by including another researcher (dietician) to conduct interviews who was not aware of the study hypothesis.

7.5.7. Statistical methodology for quantitative analysis

We approached study analysis conceptually as representing three phases of feeding choice, with potentially different factors driving change in feeding choices during transition from one to the next phase. These three phases were defined as (a) "pre-admission" (reflecting feeding choices leading up to and at the time of admission), (b) "in-hospital" (reflecting feeding choices during admission) and (c) "post-discharge" (reflecting feeding choices as reported in a later telephonic interview). We estimated prevalence of any and exclusive breastfeeding during each phase. Analogously, we evaluated change in breastfeeding practices by maternal and infant predictors for each transition (from pre-admission to in-hospital; from in-hospital to post-discharge; and from pre-admission to post discharge). In exploratory analysis, distributions were examined graphically; continuous variables were expressed as median (interquartile range, IQR) and difference in median(s) tested with Kruskal-Wallis; associations with categorical variables were examined using Chi^2 testing. We did not correct for multiplicity but used caution in overall interpretation of *p*-values. Birth weight and gestation at delivery were categorized using standard boundaries: low birth weight (LBW) was defined as birth weight <2500g, and preterm birth as <37 completed weeks' gestation. We opted to use logistic regression analysis separately for each potential transition as we hypothesised that different factors were likely to drive feeding choices in each phase. Accordingly, we analysed each transition as a cross-sectional event, with associations expressed as odds ratios (OR) or adjusted odds ratios (aOR). That is, we evaluated odds of optimal breastfeeding at admission separately to odds of cessation in hospital, and finally odds of cessation post-admission; all models included infant age as a potential confounder. We were unable to utilize time-to-event analysis as precise date of breastfeeding cessation was not available. Model building was based on best parsimonious model fit as determined by Akaike's information criterion (AIC). Potential third variables included socio-economic, maternal, admission and infant factors known to be associated with early infant feeding and chosen *a priori*. Sensitivity analysis was conducted on two subgroups of mother-infant pairs; firstly, limited to those who reported any breastfeeding during hospitalisation, and secondly, to those with infants older than six months of age at the time of post-discharge phone call.

7.5.8. Sample size considerations

Assuming pre-admission breastfeeding prevalence of 60% (based on expert opinion, PROMISE-EBF data[17] and the health indicator report from South Africa Demographic and Health Survey 2016), and 15% attrition after hospital discharge, we estimated that an initial sample size of 120 (alpha set at 0.05) would provide (1) 85% power to detect a 15% decrease in breastfeeding prevalence using univariable logistic regression; and (2) 85% power to detect a 20% decrease in breastfeeding prevalence in a multivariable model (squared multiple correlation set to 0.3).

7.5.9. Definitions

Exclusive breastfeeding (EBF): breastmilk and prescribed medicine only.

Mixed breastfeeding (MBF) or non-exclusive BF: breastmilk with other liquids or semi-solid foods. This is further divided into partial and predominant breastfeeding.

No BF: exclusive formula feeding (EFF) with no breast milk, with or without other liquids and/or solid food.

Any Breastfeeding (ABF): combination of those that EBF and practice MBF.

Complementary foods: any foodstuff, in solid or semi-solid form, given to an infant after the age of six months.

Low birth weight (LBW): a birth weight less than 2500 g.

Prematurity: babies born alive before 37 completed weeks of gestation.

7.5.10. Ethics HREC Ref: 839/2016

Patient privacy and confidentiality were respected at all costs. Data collection was anonymous and confidential. Each patient was allocated a research number. Data was collected and stored in password protected computer folders and hard copies locked in an office to which only researchers had access. No additional tests or interventions were performed on patients for the study. Informed consent was attained by mothers and translators were used where language barriers existed. There was no direct benefit and no potential harm expected for participants. This study was in accordance with the International Declaration of Helsinki and other applicable ethical codes. This study was approved by the Human Research Ethics Committee of the University of Cape Town.

7.6. Results

Overall, 119 consenting mothers were interviewed in hospital (median age 26 years, IQR 22-32; 28% HIV infected, Table 1), of whom 92 (77%) were contactable post-discharge and interviewed telephonically. Living conditions were generally challenging, with only 52% of homes having electricity plus indwelling piped water with a flush toilet. Other maternal and infant characteristics are shown in Table 1. Of the 119 hospitalised infants (median age at admission 1.8 months [IQR 1.0-3.2]), 92 had known vital status post-discharge and 3 children had demised prior to telephonic contact (Table 2). Despite losing 27 to follow up, the maternal-infant characteristics between the pre-admission and post-discharge groups did not vary meaningfully and therefore were comparable. (Table 2)

The most common primary diagnoses were lower respiratory tract infection (LRTI; n=70, 59%) and gastroenteritis (n=16, 14%; Table 1). The median duration of time between admission and in-hospital interview was 4 days (IQR 2-6) (Table 1). Telephonic follow-up interviews were conducted at a median 5 months after hospitalisation (with median infant age 6.3 months, IQR 6.0-7.5; Table 1). Among the 89 infants who were alive at follow up post-discharge, 21 (24%) were younger than or near 6 months age.

Prevalence and predictors of breastfeeding at admission

Most women (91, 77%) reported some BF prior to admission (46/91, 50% exclusively and 45/91, 50 % mixed BF), while 28 (23%) reported using infant formula +/- the introduction of early complementary feeds (EICF) without BF (Table 1). Younger infant age was strongly associated with prevalence of EBF among those women who reported any BF (Table 1, Figure 1). Significantly fewer HIV-positive (8/33, 24%) than HIV-negative mothers (38/85, 45%) reported exclusive breastfeeding (p=0.02). Overall, the majority of infants had been introduced to early complementary feeds prior to admission (73/119, 61%, Table 1).

Characteristics of children with a primary diagnosis of gastroenteritis (Table 3)

Compared to children admitted with a primary diagnosis of non-diarrhoeal diseases, those with a primary diagnosis of gastroenteritis were substantially less likely to live in homes with all amenities (25% compared to 47% of children with LRTI and 78% of children with other diagnoses, p=0.001). Specifically, 63% of children admitted with diarrhoea did not have indwelling piped water, compared to 44% of those with LRTI and 26% of those with other diagnoses (p=0.003). They were also more likely to have an HIV-positive mother (44% vs 33% LRTI and 10% other diagnoses, p=0.03), although no HIV-positive infants had been admitted with gastroenteritis. Only two children were HIV-positive; both were admitted with LRTI. Notably, none of the children admitted with gastroenteritis were EBF. In addition, all the children presenting with gastroenteritis (n=16, 100%) had been receiving solid food prior to admission compared to 56% of all other diagnoses (p=0.003) while 50% had been receiving infant formula without any BF, compared to 56% of those with LRTI and 56% of those with other diagnoses (p=0.003).

Prevalence and predictors of breastfeeding during hospitalisation

The overall prevalence of any BF declined from 77% pre-admission to 61% in hospital (supplemental table 1). However, the proportion of women in hospital who breastfed exclusively increased (from 46/119 [39%] pre-admission to 57/119 [48%] in hospital). In-

hospital milk feeding patterns correlated strongly with pre-admission milk feeding patterns. Changes in distribution of infant feeding patterns over time are shown in Figure 2.

Factors associated with breastfeeding cessation during hospitalisation (Table 4)

Of the 91 women who reported any BF pre-admission, 20 (22%) discontinued BF in hospital. Adjusting for maternal HIV, pre-admission EBF, infant age and any diagnosis of diarrhoeal illness, the odds of BF cessation were increased in infants with LBW (aOR 12.77, 95% CI 1.20-135.88; p=0.03) and those who received any bottle or tube feeding while in hospital (aOR 153.90, 95% CI 4.08-5801.66; p=0.007; table 4). Maternal expression of breastmilk was protective against in-hospital BF cessation (aOR 0.01, 95% CI 0.001-0.28; p=0.005).

Prevalence and predictors of breastfeeding post-discharge

The median infant age (N=119) at post-discharge telephonic interview was 6.3 months (IQR 6.0-7.5). Among those who were younger than 6 months at the time of the telephonic interview (n=21), 11 (52%) were still breastfeeding; and of these, 5 (24%) breastfed exclusively. Just under half of women who reported any BF prior to hospitalisation had stopped all BF by the time of telephonic interview (39/92, 42% Table 2). Women who EBF prior to or during hospitalisation were substantially more likely to maintain any BF after discharge (p<0.0001, supplemental table 1). None of the women who discontinued BF in hospital had reinitiated BF. Changes over time in overall prevalence of exclusive, mixed and no BF are shown in supplemental table 1 and Figure 2. At post-discharge, early complementary solids before 6 months of age were introduced in 38/72 (53%) of mothers practicing non-exclusive BF.

Factors associated with breastfeeding cessation at any time between admission and post-discharge telephonic interview (Table 5)

In crude and adjusted analysis, BF cessation was associated with a positive maternal HIV status (aOR 9.07, 95% CI 1.08-75.92; p=0.04), full-time employment (aOR 14.12, 95% CI 1.48-135.02; p=0.02) and prematurity (aOR 5.59, 95% CI 1.08-29.11; p=0.04) (Table 5). Pre-admission EBF was protective against BF cessation (aOR 0.06, 95% CI 0.01-0.52; p=0.01), even after adjusting for infant age, quality of paternal relationship and in-hospital feeding practices (specifically, maternal breastmilk expression and use of bottle/tube feeds).

In sensitivity analyses, restricted sample sizes resulted in loss of precision; nonetheless, point estimates and overall inferences approximated those from the main analysis (supplemental table 2).

Descriptive Data

Primary reasons for infant feeding practice at first interview by all mothers

Most mothers chose non-EBF practices because of perceptions of insufficient breastmilk. 'My breastmilk was scanty, so I stopped'. (38 years old, HIV-negative, 3-month-old infant, MBF). Other perceptions included the reluctance of the baby to breastfeed. 'She (*the infant*) didn't want it *(breastmilk)*. (21 years old, HIV-negative, 3-month-old infant, MBF)

Other reasons why mothers chose non-EBF practices was because of employment. 'I had to go back to work. Told to breastfeed by nursing staff. Was going to breastfeed for 6 months then I got work - had no choice. Takes long to express and fill a cup. Bought *(BMS)* to help.' (28 years old, HIV-negative, 5-month-old infant, introduced BMS to infant at 3 months of age)

Importantly, reasons reported for non-EBF practices included ambiguity about the benefits of BF compared to using BMS. 'Formula milk is best for the baby. Vomiting with breastmilk.' (28 years old, HIV-positive, 3-month-old infant, MBF). Mothers also assumed that breastmilk was similar to BMS.'*(BMS)* is like mothers' milk. (18 years old, HIV-negative, 2-month-old infant, MBF)

HIV-positive mothers expressed concerns regarding HIV transmission. 'I do not want to risk giving my child the disease *(HIV)*.' (31 years old, 1-month HEU infant, EFF) Or they were too ill to breastfeed. 'I bled too much after giving birth, I was weak. The doctors said I cannot give the breast. I had a Pulmonary Embolism.' (26 years old, 3-month-old HEU infant, EFF). Some HIV-positive mothers were pressured by others when reporting their concerns with their infant or when seeking general breastfeeding support. '*(I use BMS)* because *(my infant is)* not going to toilet *(stooling)*. (39 years old, 2-month-old HEU infant, advised by HCW, MBF)

Responses from mothers who practiced mixed or exclusive breastfeeding while in hospital but were not expressing breastmilk.

Mothers expressed content with their experiences and support provided in the general paediatric wards. Some mothers were taught how to express breastmilk by HCW's at their birthing facilities or by HCW's in the PICU of RCWMCH. '*(HCW)* gave me a lot of support… very helpful and good follow up. I have a lot of confidence to go back to breastfeeding.' (17 years old, HIV-negative, 1.5-month-old infant)

Some mothers felt pressured at the prescribed quantities of expressed breastmilk required. 'She *(infant)* feeds a lot therefore not enough *(breastmilk)* when I express. A lot of effort for nothing.' (23 years old, HIV-negative, 3-month-old infant).

Mothers also felt that they were not adequately supported. 'Tried to express and cup feed but was given a bottle.' (Unknown maternal age, HIV-negative, 1-month old infant). Some mothers were given mixed messages. 'I discard it *(expressed breastmilk)* because told cannot breastfeed if I am HIV.' (Unknown maternal age, HIV-positive, 2-month-old HEU infant).

7.7. Discussion

Our study showed a low EBF prevalence of 39% in infants younger than six months at the time of admission, followed by a slight increase in EBF prevalence to 48% during hospitalisation, with an even lower EBF prevalence of 24% in children younger than six months post discharge from RCWMCH. These results fall within the range of EBF estimates in the latest South African Demographic and Health Survey (32%) and suggest an ongoing and unacceptably low prevalence of EBF in young South African infants.

Predictors of exclusive breastfeeding at admission included a younger infant age, maternal report of a good relationship with the infants' father, and an HIV-negative maternal status. The majority of infants in our study were introduced to early complementary feeds before hospitalisation (73/119, 61%) which is consistent with previous research.[31] Being a single parent and/or having a poor relationship with the father of the infant were also associated with early complementary feeding prior to hospitalisation. In keeping with other studies, our data suggest that household family members, particularly grandmothers, are influential in infant feeding practice and do not always support EBF or follow policy. [9,12,14] Where paternal support was poor or absent, single mothers turned to their own mothers (infant grandmothers) for infant feeding advice despite their knowledge and intention to EBF. [9]

Changes in infant feeding choices were common during hospitalisation, including a higher proportion of infants reported as EBF. Simultaneously, the overall prevalence of any BF declined. These changes may reflect the influence of HCW advice against mixed feeding. Prior to the widespread availability of maternal ART, mixed feeding was particularly discouraged in the context of HIV, and it is possible that the fear of HIV transmission previously associated with mixed feeding still influences HCW advice regarding infant feeding. Therefore, possible explanations are mothers' fear of judgement of mixed feeding by HCW, but also, having to stay with their infant 24/7 would make it easier for those back at work, and perhaps knowing EBF is important for the health of the infant might make the mother want to EBF more.

Early cessation of breastfeeding was common in the study population, both during and after hospitalisation. HIV-positive mothers were more likely to have discontinued BF early, before six months (p=0.04). Previous research suggests that these mothers face multiple challenges in sustaining optimal and exclusive infant feeding practices due to inconsistent advice from HCWs [10] and the inadvertent contradictory messaging from the PMTCT's free formula provision initiative and the stigma surrounding it. [20] Our results indicated a positive association between maternal HIV-infection and infant hospitalisation with gastroenteritis. This is in keeping with other research that has suggested increased risks of hospitalisation and infectious illness among HIV-exposed uninfected (HEU) compared to HIV-unexposed infants. [11,32] In the context of early breastfeeding cessation among HIV-positive women, it is however not possible to conclude to what degree these associations are driven by HIV-positive mothers' suboptimal infant feeding practices (25/33, 76%).

Breastfeeding cessation in hospital was associated with low birth weight and any bottle or tube feeding. Indeed the proportion of LBW infants who were EBF at admission was extremely low, at 26%.The majority of LBW infants in our cohort were admitted for diagnoses relating to prematurity or failing to thrive (FTT), suggesting that this group of vulnerable infants had not been adequately BF since birth and had not gained adequate

weight resulting in the early introduction of complementary feeds and no mothers who discontinued BF in hospital reinitiated BF after discharge.

In-hospital feeding practices were associated with risk of breastfeeding cessation. For example, those who received bottle or tube feeding were at increased risk of cessation while maternal expressing of breastmilk was protective against cessation of breastfeeding in hospital. Unfortunately, less than half of BF mothers reported any expressing during admission. It is recognised that the use of bottles (or ready-made bottled formula) may be temporarily required for medical reasons when a sick infant is unable to BF or requires specialised nutrition, and when mothers are absent. However, the in-hospital use of bottles is not supported by the MBFI and its use for sick infants provides mixed messaging to mothers.

In our study, almost all mothers roomed in (98%) and almost half also made use of the lodging facilities (42%). This meant that mothers were almost always available in the ward and on occasion contactable within the hospital premises, yet this did not impact positively on BF practice or breastmilk expressing in hospital. A retrospective study from India showed that regular breastfeeding counselling (BFC) for mothers of hospitalised infants less than 6 months improved their breastfeeding status irrespective of their feeding practice at home.[33] RCWMCH does not have a dedicated BFC team and, to date, the ward HCW's are not providing this service in the wards.

Factors associated with suboptimal infant feeding practices post discharge were largely similar to those during and before admission. Mothers with premature infants were more likely to have discontinued BF at any time between hospitalisation and post-discharge and they were also less likely to EBF at presentation. Premature infants are at increased risk of death outside the neonatal period, once discharged home from birthing facilities, thought to be secondary to preventable infections like LRTIs.[30] Of those infants hospitalised with LRTI in our study cohort, just over a third (36%, n=25/70) were premature. Suboptimal BF practice in premature infants could be another influential factor contributing to the high post-neonatal morbidity and mortality.

Full-time employment was associated with BF cessation before six months (p=0.02) and it is a barrier to EBF because mothers need to return to work (or look for employment) and workplace protections, such as adequate maternity and breastfeeding breaks are not supported. [2,12]

Only half (52%) of households in our study had all three household amenities, including indwelling piped water, electricity and a flushing toilet. Specifically, and above national statistics of 42%, [34] almost two thirds of households (63%) in our study did not have indwelling piped water, making BMS preparations hazardous. Infants who formula feed during the first six months of life are at increased risk of morbidity and mortality from unsafe water, inadequate formula preparation or storage and formula shortages, particularly in low resource settings.[35]

No infants admitted with gastroenteritis were EBF and the most common reasons for hospitalisation were LRTIs and gastroenteritis, causes known to be associated with lack of breastfeeding. [35] Further supporting evidence suggests that suboptimal infant feeding practices such as early complementary feeds or shorter duration of EBF, regardless of maternal HIV status, are all associated with increased infant morbidity. [15] Where effective

maternal ART is available, extended BF can be supported as this would reduce infant mortality without incurring increased postnatal mother-to-child transmission (MTCT).

Our study shows that hospitalisation adversely affects BF success. Mothers with HIV, full-time employment, mothers of LBW/premature infants and those who received any bottle or tube feeding in-hospital are significantly at risk of stopping breastfeeding early (before six months). These mothers require a continuum of care starting from antenatal counselling and nutritional support right through admission to post-natal community-based infant feeding support and an enabling work environment to BF. In-hospital use of bottles should be discouraged and replaced with cups for temporary delivery of feeds. Breastmilk expression was protective against BF cessation which implies the need for more in-hospital training about lactation and BF support amongst HCW staff.

7.8. Strengths and Limitations

Our feeding measures may be subject to recall and misclassification bias. Ideally, questionnaires related to infant feeding practices should be based on 24-hour or 7-day recall with detailed, structured and specific questions and administered in a formally translated format. However, we were limited in the availability of time for interviews and funding for formal translation. In the context of maternal HIV infection with pressure from HCW, it is possible that maternal responses regarding exclusivity may have been influenced by social desirability bias. However, any differential misclassification of infant feeding is unlikely to occur within the same mother-infant pairs over time Nonetheless, our data should be interpreted with these limitations in mind. The repeated measures of infant feeding over time to assess dynamic alteration in feeding patterns peri-hospitalisation is a major strength of our study. Additionally, our findings are novel as few data are available on longitudinal BF practices of young infants during and after hospitalisation. The combination of quantitative and qualitative methods, and detailed examination of socio-economic and relational factors further strengthen our results.

The lack of a non-hospitalised comparison group prevents attribution of causality in peri-hospitalisation infant feeding changes, and residual confounding is likely. Nonetheless, we provide compelling evidence of the longer-term importance of in-hospital infant feeding patterns regardless of causality.

The study location was a large, paediatric tertiary care centre which receives sub-specialty referrals from across SA and has a large intensive care unit. Our data may not be generalisable to other settings or levels of care. Inpatients often have severe spectrums of disease, requiring intensive nursing care therefore the nursing staff in our setting may have less capacity to support optimal BF practices than those in secondary level hospitals. Nonetheless, the primary diagnoses most common in our study population were common infectious childhood illnesses.

Due to convenience sampling, our data may also be subject to selection bias. We were only able to include mothers who were by their infants' bedside and telephonically contactable. As such, our population may overrepresent women of relatively better socio-economic situation. Given the associations of suboptimal BF with poor socio-economic situation demonstrated in our data, we may therefore have underestimated the true prevalence of suboptimal infant feeding practices in our wards. Simultaneously, this data is not generalisable to the surrounding communities. Optimal BF is protective against both incidence and severity of diarrhoeal and respiratory illness; therefore, suboptimal BF practices are likely to be overrepresented among children hospitalised for these diseases. Attrition was higher than anticipated; consequently, the study is underpowered for sub-group analyses and there is risk for selection bias due to differential loss to follow-up.

The study did not include healthcare worker practices and support for breastfeeding within this context. This information is needed in motivating for a mother-baby friendly hospital context in which there will be policy implementation and support for breastfeeding babies. From this perspective, our study could serve as springboard for funding to measure and improve HCW practices related to infant feeding during admission.

7.9. Conclusion

In our study, prevalence of both any and exclusive BF was unacceptably low on admission to hospital, and a lack of BF strongly correlated with increased risk of an infectious morbidity diagnosis. In addition, hospitalisation independently and substantially reduced the probability of continued BF. EBF is a life-saving and wellness-promoting intervention throughout the life course for all children in SA. Interventions to optimize BF prevalence and duration are critical for improving child survival. Urgent interventions are required to support BF during infant hospitalisation to RCWMCH. BF and breastmilk expression support by medical staff in-hospital during an infant's temporary inability to BF should be improved. Further research is required to define optimum in-hospital BF support practices in SA.

7.10. Recommendations

EBF prior to hospitalisation was protective against BF cessation even after adjusting for in-hospital breastmilk expression and the use of bottles and/or tube feeds (p=0.01). Hospitalisation should be viewed as an imperative window of opportunity to reinforce EBF, support extended BF practices and help mothers re-initiate BF. Further implementation research may define additional effective in-hospital BF support interventions

HIV-positive mothers chose MBF or no BF because of fear of transmission (15%) but mainly because of the need to return to work (28%) and alarmingly because of HCW advice (20%). HCWs are still influenced by the old messaging for feeding in the context of HIV. Even if staff members have been trained, many continue to counsel HIV-positive mothers not to BF, but rather to use formula milk. Again, this reinforces the urgent need to implement more MBF hospitals which commit to the provision of quality counselling on infant feeding in the context of HIV.

Considering that 80-90% of infants leave birthing facilities EBF, this study's low EBF prevalence at a younger infant age of two months (39%) and remarkably low proportion of HIV-exposed BF babies (19/33, 58%), suggest the need to increase emphasis on continued BF support for mothers (and families) within the community.

7.11. References for publication-ready manuscript

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7.12. Tables and Figures

TABLE 1. Baseline characteristics of mother-infant pairs pre-admission by infant feeding practices

	Total N=119	Exclusive breastfeeding n=46	Mixed breastfeeding n=45	No breastfeeding n=28	*p*- value
Maternal characteristics					
Age (years)	26 (22-32)	28 (24-32)	25 (21-29)	29 (23-35)	0.10
Mother < 26 years old	53 (47%)	19 (43%)	25 (57%)	9 (38%)	0.24
Completed ≥ grade 8 in school	110 (94%)	44 (96%)	42 (95%)	24 (89%)	0.44
Employment full-time	23 (19%)	6 (13%)	12 (27%)	5 (18%)	0.25
HIV-positive	33 (28%)	8 (17%)	11 (24%)	14 (50%)	0.02
Marital Status					0.002
Single parent	45 (38%)	10 (22%)	18 (40%)	17 (61%)	
Co-parenting, not married	27 (23%)	9 (20%)	12 (27%)	6 (21%)	
Married	46 (39%)	27 (59%)	15 (33%)	4 (14%)	
Good relationship with child's father	75 (63%)	40 (87%)	24 (53%)	11 (39%)	<0.0001
Primary language					0.007
Xhosa	60 (50%)	15 (33%)	27 (60%)	18 (64%)	
Afrikaans	23 (19%)	8 (17%)	8 (18%)	7 (25%)	
English	19 (16%)	12 (26%)	6 (13%)	1 (4%)	
Other	16 (14%)	11 (24%)	4 (9%)	1 (4%)	
Home has all amenities[1]	62 (52%)	27 (59%)	22 (49%)	13 (46%)	0.51
Infant Characteristics					
Gestation at birth (weeks)	38 (36-40)	38 (38-40)	38 (36-40)	37 (35-39)	0.73
Preterm (<37 weeks)	41 (34%)	15 (33%)	15 (33%)	11 (39%)	0.83
Birth weight (kg)	2.8 (2.2-3.2)	3.0 (2.5-3.2)	2.8 (2.2-3.3)	2.6 (1.9-3.2)	0.57
Low birth weight (<2500g)	39 (33%)	10 (22%)	18 (41%)	11 (41%)	0.10
Male sex	64 (54%)	24 (52%)	24 (53%)	16 (57%)	0.91
HIV status					0.02
Unexposed, uninfected	87 (73%)	38 (83%)	35 (78%)	14 (50%)	
Exposed, uninfected	28 (23%)	8 (17%)	7 (16%)	13 (46%)	

	Total N=119	**Exclusive breastfeeding n=46**	**Mixed breastfeeding n=45**	**No breastfeeding n=28**	***p*- value**
Exposed, infected	2 (2%)	0	1 (2%)	1 (4%)	
Unknown	2 (2%)	0	2 (4%)	0	
Primary diagnosis at admission					0.008
Gastroenteritis	16 (14%)	0	8 (18%)	8 (29%)	
Lower Respiratory Tract Infection	70 (59%)	31 (69%)	24 (53%)	15 (54%)	
Other	32 (27%)	14 (31%)	13 (29%)	5 (18%)	
Infant age (months)	1.8 (1.0-3.2)	1.1 (0.8-1.8)	2.6 (1.5-3.6)	2.4 (1.4-4.2)	0.0001
Receives solid food	73 (61%)	0	45 (100%)	28 (100%)	n/a
Infant characteristics at second interview in hospital	**N=119**	**n=46**	**n=45**	**n=28**	
Time in hospital prior to second interview (days)	4 (2-6)	3 (1-4)	3 (2-7)	5 (3-7)	0.03
Post-discharge characteristics	**N=89**	**n=37**	**n=32**	**n=20**	
Infant age at post-discharge telephonic interview (months)	6.3 (6.0-7.5)	6.0 (5.5-6.4)	7.0 (6.0-7.8)	7.5 (6.1-8.5)	0.001
Time since in-hospital interview (months)	4.6 (4.2-5.2)	4.6 (4.4-5.1)	4.5 (4.1-5.1)	4.3 (3.9-5.3)	0.36

Data are number (%) except in heading; or median (interquartile range, IQR), categorical variables tested with chi^2; continuous variables with Kruskal-Wallis; *p*-values not corrected for multiplicity

[1] "All amenities" defined as having all three of: indwelling flush toilet; indwelling piped water and electricity

Missing maternal data: age, n=7; HIV status, n=1; marital status, n=1; relationship with child's father, n=2; primary language, n=1; Missing infant data: birth weight, n=2; infant age at interview, n=1; HIV status, n=2

TABLE 2. Maternal and infant characteristics by vital status and availability at time of telephonic contact

	Telephonic interview completed (N=92)		Telephonic interview not completed (N=27)	*p*-value
	Alive (n=89)	Deceased (n=3)		
Mother older than 26 years	45 (54%)	2 (67%)	12 (46%)	0.68
HIV positive	24 (27%)	0	9 (33%)	0.75
Good relationship with child's father	57 (64%)	2 (67%)	16 (59%)	0.91
Completed grade 8 or higher	83 (95%)	3 (100%)	24 (89%)	0.42
Full-time employment	19 (21%)	1 (33%)	3 (11%)	0.41
Home does not have all amenities	43 (48%)	1 (33%)	13 (48%)	0.88
Infant feeding pre-admission				0.47
Exclusive breastmilk	37 (42%)	2 (67%)	7 (26%)	
Mixed breastmilk	32 (36%)	1 (33%)	12 (44%)	
Formula, no breastmilk	20 (22%)	0	8 (30%)	
Preterm (< 37 weeks)	33 (37%)	1 (33%)	7 (26%)	0.57
Low birth weight (< 2500g)	26 (30%)	2 (67%)	11 (42%)	0.22
Male sex	51 (57%)	1 (33%)	12 (44%)	0.39
Infant HIV status				0.81
Unexposed, uninfected (HUU)	66 (74%)	3 (100%)	18 (67%)	
Exposed, uninfected (HEU)	21 (24%)	0	7 (26%)	
Exposed, infected (HEI)	1 (1%)	0	1 (4%)	
Infant age at admission (months)	1.7 (1.0-2.9)	1.1 (0.9-5.2)	2.0 (1.2-3.8)	0.70
Primary diagnosis				0.19
Gastroenteritis	11 (12%)	0	5 (19%)	
Lower respiratory tract infection	55 (62%)	0	15 (56%)	
Other	23 (26%)	3 (100%)	7 (26%)	

Numbers are n (column %); categorical variables tested with chi2, continuous with Kruskal- Wallis; no correction for multiplicity; All amenities defined as all three of: indwelling flush toilet; indwelling piped water and electricity
Missing data, maternal: Maternal age, n=7; HIV status, n=1
Missing data, infant: Birth weight, n=2; infant age at interview, n=1; HIV status, n=2; Marital status, n=1; Relationship with child's father, n=2; primary diagnosis, n=1

TABLE 3. Maternal and infant characteristics in hospital by primary diagnosis

	PRIMARY DIAGNOSIS			
	Gastroenteritis (N=16)	**Lower respiratory tract infection (N=70)**	**Other (N=32)**	***p*-value**
Maternal & household				
Maternal HIV infection	7 (44%)	23 (33%)	3 (10%)	0.03
Has all amenities (indwelling piped water plus flush toilet plus electricity)	4 (25%)	33 (47%)	25 (78%)	0.001
Specific lack of amenities				
No electricity	2 (15%)	2 (3%)	1 (3%)	0.22
No indwelling, piped water	10 (63%)	30 (44%)	5 (26%)	0.003
No indwelling, flush toilet	10 (63%)	29 (42%)	6 (19%)	0.01
Pre-admission infant feeding patterns				
Infant milk feeding				
Exclusive breastmilk	0	31 (44%)	14 (44%)	0.008
Mixed breastmilk (± formula)	8 (50%)	24 (34%)	13 (41%)	
Formula, no breastmilk	8 (50%)	15 (21%)	5 (16%)	
Infant receives solid food	16 (100%)	39 (56%)	18 (56%)	0.003
Birth & infant				
Low birth weight (<2500g)	4 (27%)	26 (37%)	9 (29%)	0.61
Preterm (<37 weeks)	5 (31%)	25 (36%)	11 (35%)	0.94
Infant HIV exposure and infection status				
HIV-unexposed, uninfected	9 (56%)	48 (69%)	29 (91%)	0.11
HIV-exposed, uninfected	6 (38%)	19 (27%)	3 (10%)	
HIV-exposed, infected	0	2 (3%)	0	
Unknown	1 (6%)	1 (1%)	0	

Numbers are n (column %); p-values from chi^2 testing without correction for multiplicity Missing data: Primary diagnosis, n=1; Maternal HIV status, n=1; Birth weight, n=2; Infant HIV status, n=2; Amenities, n=2

TABLE 4. Predictors of breastfeeding cessation in hospital, among breastfeeding mothers at admission (N=91): crude and adjusted odds ratios from logistic regression analysis

	Crude logistic regression			Adjusted logistic regression		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Maternal characteristics						
Maternal age >26 years[1]	1.00	0.37-2.71	1.00	-	-	-
HIV-positive[2]	3.58	1.19-10.76	0.02	1.39	0.19-10.02	0.74
Completed grade 8 or higher[3]	0.85	0.08-8.66	0.89	-	-	-
Employed full-time[4]	2.11	0.67-6.59	0.20	-	-	-
Household has all amenities[5]	0.49	0.18-1.34	0.16	-	-	-
Poor relationship with child's father[6]	1.82	0.65-5.15	0.26	-	-	-
Infant characteristics						
Exclusive breastfeeding pre-admission[7]	0.07	0.01-0.32	0.001	3.10	0.16-60.35	0.45
Infant age at interview (months)	2.18	1.43-3.32	<0.0001	1.34	0.66-2.70	0.42
Preterm birth (<37 weeks)[8]	1.48	0.54-6.36	0.33	-	-	-
Low birth weight (<2500 g)[9]	3.81	1.35-10.74	0.01	12.77	1.20-135.88	0.03
Male sex[10]	0.67	0.25-1.82	0.43	-	-	-
Admission characteristics						
Primary diagnosis						
Gastroenteritis	Ref	Ref	-	-	-	-
Lower respiratory tract infection	0.13	0.03-0.65	0.01	-	-	-

	Crude logistic regression			Adjusted logistic regression		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Other	0.14	0.02-0.77	0.02	-	-	-
Any diarrhoeal illness in diagnoses[11]	5.58	1.34-23.31	0.02	8.88	0.55-144.16	0.13
Mother expresses breastmilk in hospital[12]	0.07	0.01-0.33	0.001	0.01	0.001-0.28	0.005
Mother rooming in[13]	0.27	0.02-4.54	0.36	-	-	-
Mother uses/has access to lodging[14]	0.68	0.24-1.90	0.46	-	-	-
Infant fed with bottle and/or tube[15]	51.00	6.38-407.71	<0.0001	153.90	4.08-5801.66	0.007
Days between admission and interview	1.53	0.84-2.80	0.16	-	-	-

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval

1 Compared to mothers younger than 26 years; 2 Compared to HIV-uninfected mothers; 3 Compared to mothers who did not complete at least Grade 8; 4 Compared to mothers who were unemployed, employed part-time or students; 5 Compared to those with less than three of: indwelling piped water; indwelling flush toilet; and electricity; 6 Compared to mothers who reported a good relationship with index child's father; 7 Compared to mixed breastfeeding, based on maternal recall; 8 Compared to term infants (born at or after 37 weeks completed gestation); 9 Compared to infants with birth weight of 2500g or greater; 10 Compared to female infants; 11 Compared to infants who did not have diarrhoeal illness as part of any in-hospital diagnosis prior to interview; 12 Compared with those who did not; 13 Compared to those who did not sleep in room with infant; 14 compared to those who did not qualify for or chose not to use hospital lodging facilities; 15 compared to cup and/or breastfeeding

TABLE 5

Predictors of breastfeeding cessation <u>at any time before post-discharge telephonic interview</u> (N=69 women who were breastfeeding at admission and also available for telephonic interview post-discharge): crude and adjusted odds ratios from logistic regression analysis

	Crude logistic regression			Adjusted logistic regression		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Maternal characteristics						
Maternal age >26 years[1]	1.29	0.49-3.39	0.61	-	-	-
HIV-positive[2]	2.82	0.84-9.40	0.09	9.07	1.08-75.92	0.04
Completed grade 8 or higher[3]	2.65	0.26-26.82	0.41	-	-	-
Employed full-time[4]	4.95	1.40-17.46	0.01	14.12	1.48-135.02	0.02
Household has all amenities[5]	0.86	0.33-2.24	0.76	-	-	-
Poor relationship with child's father[6]	3.54	1.15-10.87	0.03	3.01	0.51-17.61	0.22
Infant characteristics						
Exclusive breastfeeding pre-admission[7]	0.07	0.02-0.21	<0.0001	0.06	0.01-0.52	0.01
Infant age at telephonic interview, post-discharge (months)	1.51	0.98-2.33	0.06	0.85	0.40-1.80	0.66
Preterm birth (<37 weeks)[8]	3.53	1.27-9.81	0.02	5.59	1.08-29.11	0.04
Low birth weight (<2500 g)[9]	2.83	0.96-8.40	0.06	-	-	-
Male sex[10]	1.09	0.42-2.83	0.86	-	-	-
Admission characteristics						
Primary diagnosis						

	Crude logistic regression			Adjusted logistic regression		
	OR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Gastroenteritis	Ref	Ref	-			
Lower respiratory tract infection	0.12	0.01-1.11	0.06	-	-	-
Other	0.24	0.02-2.49	0.23	-	-	-
Any diarrhoeal illness in diagnoses[11]	3.24	0.58-18.01	0.18	-	-	-
Mother expresses breastmilk in hospital[12]	0.59	0.22-1.55	0.28	0.34	0.06-1.94	0.23
Mother uses/has access to lodging[13]	1.10	0.42-2.87	0.84	-	-	-
Infant fed with bottle and/or tube[14]	7.14	2.40-21.25	<0.0001	2.10	0.24-18.49	0.50
Time since discharge (months)	0.65	0.30-1.41	0.28	-	-	-

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval

1 Compared to mothers younger than 26 years; 2 Compared to HIV-uninfected mothers; 3 Compared to mothers who did not complete at least Grade 8 ; 4 Compared to mothers who were unemployed, employed part-time or students; 5 Compared to those with less than three of: indwelling piped water; indwelling flush toilet; and electricity; 6 Compared to mothers who reported a good relationship with index child's father; 7 Compared to mixed breastfeeding, based on maternal recall; 8 Compared to term infants (born at or after 37 weeks completed gestation); 9 Compared to infants with birth weight of 2500g or greater; 10 Compared to female infants; 11 Compared to infants who did not have diarrhoeal illness as part of any in-hospital diagnosis prior to interview; 12 Compared with those who did not; 13 compared to those who did not qualify for or chose not to use hospital lodging facilities; 14 compared to cup and/or breastfeeding

SUPPLEMENTAL TABLE 1. Relationships between pre-admission, in-hospital and post-discharge infant milk feeding

6 (a) Associations between pre-admission and in hospital feeding					
	In hospital infant feeding (N=119)				
	EBF (n=57)	MBF (n=15)	No BF (n=47)	Missing (n=0)	
Pre-admission (N=119)					*p*-value
EBF (n=46)	40 (87%)	4 (9%)	2 (4%)	-	
MBF (n=45)	16 (36%)	11 (24%)	18 (40%)	-	<0.0001
No BF (n=28)	1 (4%)	0	27 (96%)	-	

6 (b) Associations between pre-admission and post-discharge feeding				
	Post-discharge (N=119)			
	Any breastfeeding (n=37)	No BF (n=52)	Missing (n=30)	
Pre-admission (N=119)				*p*-value
EBF (n=46)	30 (65%)	7 (15%)	9 (20%)	
MBF (n=45)	7 (16%)	25 (56%)	13 (29%)	<0.0001
No BF (n=28)	0	20 (71%)	8 (29%)	

6 (c) Associations between in-hospital and post-discharge feeding				
	Post-discharge (N=119)			
	Any breastfeeding (n=37)	No BF (n=52)	Missing (n=30)	
In hospital (N=119)				*p*-value
EBF (n=57)	33 (58%)	13 (23%)	11 (19%)	
MBF (n=15)	4 (27%)	7 (46%)	4 (27%)	<0.0001
No BF (n=47)	0	32 (68%)	15 (32%)	

Numbers are n (row %); *p*-values from chi^2 tests without correction for multiplicity.
Abbreviations: EBF, exclusive breastfeeding (breastmilk and prescribed medicine only); MBF, mixed breastfeeding (Breastmilk with any other liquids or solid food); No BF (Formula feeding with no breast milk, with or without other liquids and/or solid food); infant feeding categories based on maternal recall

SUPPLEMENTAL TABLE 2. Sensitivity analysis: predictors of breastfeeding cessation post-discharge for (1) all breastfeeding mothers at admission (2) restricted to breastfeeding mothers at admission who continued breastfeeding through hospitalisation and (3) restricted to breastfeeding mothers at admission with infants 6 months or older at post-discharge telephonic interview

	(1) Breastfed at admission N=91			**(2) Breastfed at admission and continued in hospital N=72**			**(3) Breastfed at admission and infant ≥6 months at post-discharge telephonic interview N=37**		
	aOR	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
HIV-positive mother[1]	9.07	1.08-75.92	0.04	7.79	0.83-72.85	0.07	7.06	0.53-93.26	0.14
Mother employed full-time[2]	14.12	1.48-135.02	0.02	13.56	1.37-133.95	0.03	6.51	0.45-93.44	0.17
Poor relationship with child's father[3]	3.01	0.51-17.61	0.22	4.07	0.67-24.65	0.13	0.95	0.12-7.66	0.96
Exclusive breastfeeding pre-admission[4]	0.06	0.01-0.52	0.01	0.09	0.01-0.74	0.03	0.05	0.003-0.81	0.04
Infant age at telephonic interview (months)	0.85	0.40-1.80	0.66	0.85	0.40-1.80	0.67	0.81	0.36-1.80	0.60
Preterm birth (<37 weeks)[5]	5.59	1.08-29.11	0.04	5.43	0.97-30.24	0.05	11.70	1.31-104.18	0.03
Mother expresses breastmilk in hospital[6]	0.34	0.06-1.94	0.23	0.56	0.09-3.54	0.54	0.16	0.02-1.37	0.09
Infant fed with bottle and/or tube[7]	2.10	0.24-18.49	0.50	1.34	0.14-11.85	0.83	2.63	0.20-34.37	0.46

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; 1 Compared to HIV-uninfected mothers; 2 Compared to mothers who were unemployed, employed part-time or students; 3 Compared to mothers who reported a good relationship with index child's father; 4 Compared to mixed breastfeeding, based on maternal recall; 5 Compared to term infants (born at or after 37 weeks completed gestation); 6 Compared with those who did not; 7 compared to cup and/or breastfeeding

FIGURE 1

Distribution of infant age at admission by infant feeding categories

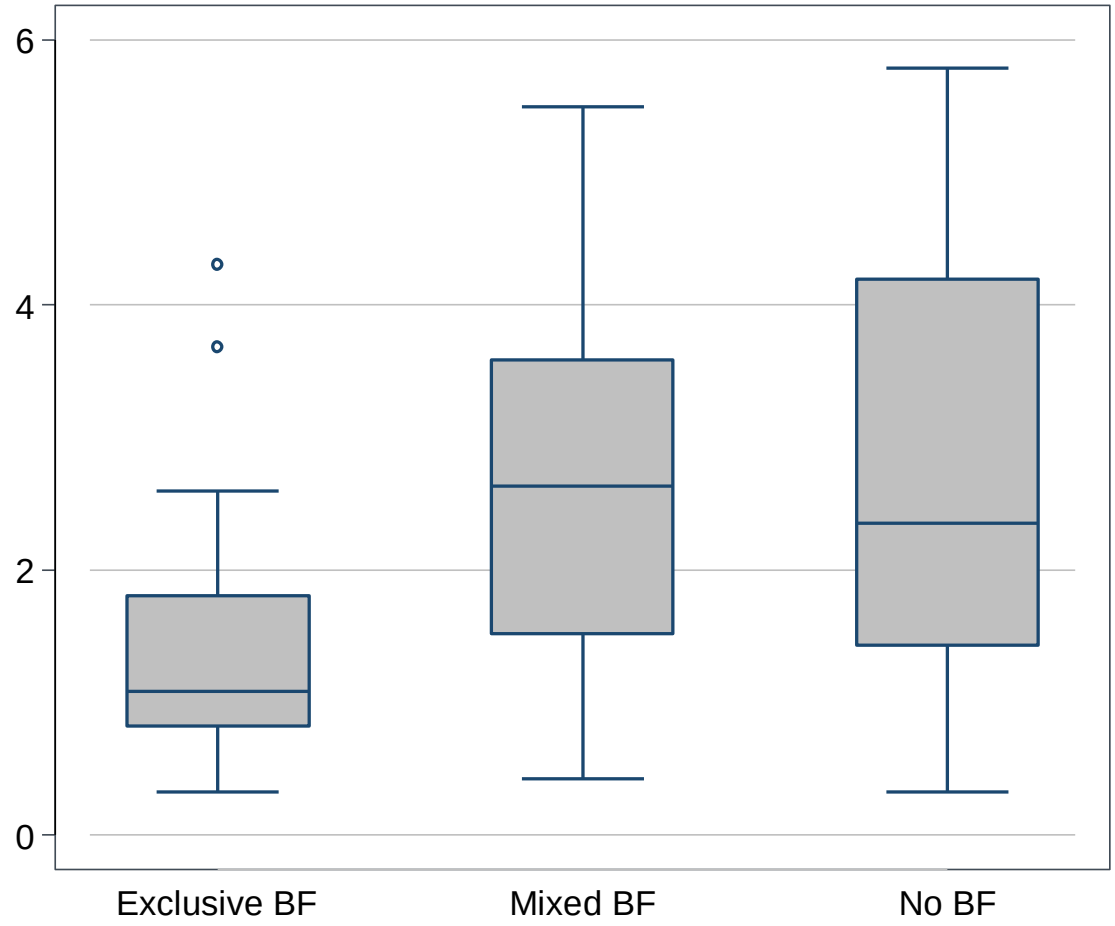
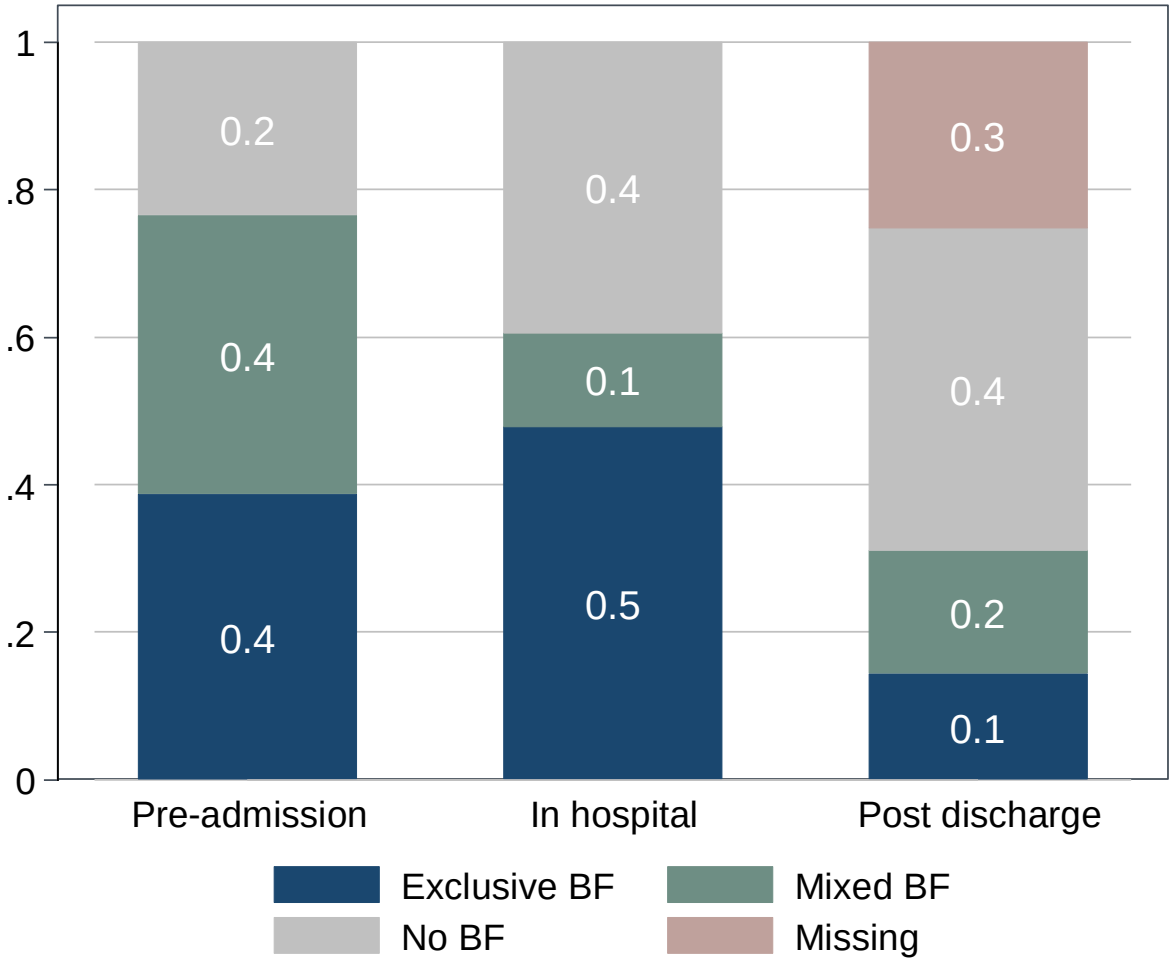


FIGURE 2

Distribution of infant feeding patterns over time



8. Appendices

8.1 Appendix 1 : The Study Protocol

Adverse impact of hospitalisation on infant breastfeeding practices: a prospective cohort study.

Student: Michelle Rina Alisio

ALSMIC001

Research Protocol

Submitted as part of the fulfilment of requirements for the degree

Master of Medicine (MMed) Paediatrics

University of Cape Town
Faculty of Health Sciences
Supervisors: Prof Christiaan Scott
Dr Stuart Maxwell Kroon

Department of Paediatric Critical Care, Red Cross War Memorial Children's Hospital

Adverse impact of hospitalisation on infant breastfeeding practices: a prospective cohort study.

Aim: To compare feeding practices of infants less than six months of age before and after hospitalisation to tertiary care

Objectives:

1. Pre-hospitalisation
   - To determine breastfeeding proportion of infants less than 6months of age hospitalised to Red Cross War Memorial Children's Hospital (RCWMCH), who breastfed exclusively
   - Identify factors associated with exclusive breastfeeding
   - Determine reasons for feeding choices and what alternatives are being used.
2. During hospitalisation
   2a. Determine proportion who breastfed during admission
   2b. Determine lodging arrangement during admission
   2c. Open ended: In hospital barriers and experience of mothers
3. At follow up
   - What proportion are breastfeeding approximately one month after discharge.

Literature review

Breastfeeding improves the survival, health and development of all children[1513]. It also saves women's lives through the protection against non-communicable diseases such as breast cancer and diabetes[1].The promotion of exclusive breastfeeding (EBF) for the first six months of life is potentially one of the top interventions for reducing under -5 child mortality[132]and the most cost-effective measure to reduce infant morbidity and mortality in low income settings[13]. Despite its established benefits, breastfeeding is no longer the norm in many communities[13]. In South Africa (SA), national breastfeeding rates at six months are estimated at 6.8 – 8.3%[3]. Concurrently, infant and child mortality rates remain high[1513].

The successful protection, promotion, and support of breastfeeding needs mobilisation of measures at many levels[2]. The hospital setting and services is one level where families and communities can be supported to breastfeed optimally[2]. Evidence has shown that the Breastfeeding Friendly Hospital Initiative (BFHI) has improved breastfeeding rates[2], however information about breastfeeding from many countries worldwide is not available[1].

The role of breastfeeding in HIV transmission and the knowledge surrounding this issue has evolved over the past two decades[8]. In South Africa, where child mortality rates are among the highest in the world, HIV infection is common and a leading cause of death[36]. Mixed feeding, also referred to as partial breastfeeding, in both HIV exposed and HIV unexposed infants, is less protective against illnesses such as pneumonia and gastroenteritis than exclusive breastfeeding[36]. However, although exclusive breastfeeding provides the greatest benefits for both mothers and infants, even any breastfeeding is associated with improved survival when compared to no breastfeeding[1]. The HIV exposed uninfected (HEU) infant

population is growing and may be at increased risk of severe infections in the first year of life[32]. Breastfeeding HEU infants have been shown to have a significantly lower risk of diarrhoea and hospitalisation at three months[37]. The World Health Organisation (WHO), the Tshwane Declaration for Breastfeeding 2011 and other international agencies acknowledge the evidence that anti-retrovirals (ARVS) significantly reduce the risk of HIV transmission through breastfeeding[15837]. In particular, suppressive maternal anti-retroviral therapy minimises the risk of transmission even if breastfeeding is partial. In a resource -limited setting, where ARV's are available, HIV positive mothers should breastfeed[837].

Breast-feeding is an important determinant of infant health in the prevention of malnutrition and infection[38]. In resource limited settings, where child mortality due to diarrhoea, pneumonia and malnutrition is common, the compounding factor of immunodeficiency makes feeding practices amongst all infants a very important focus[15]. Worldwide, diarrhoea and pneumonia remain two of the main preventable causes of death in children under five years[151]. These are two of the top main reasons for hospitalisation to RCCWMH seen by a 6month audit in 2015[39]. Overwhelming evidence from low and middle income countries show that breastfeeding protects against malnutrition, diarrhoea and respiratory infections[15] [40].

Various social, psychological, emotional and environmental factors determine whether an infant is breastfed or formula fed[1] [18]. Common reasons frequently cited by mothers worldwide is the need to return to work and the perception of breastmilk insufficiency[18]. A mother's perceived lack of confidence in her breast- feeding ability, promoted by infant crying behaviour, means that she may be easily persuaded to introduce formula milk by the aggressive marketing and easy availability of breastmilk substitutes. Breastmilk substitutes are a multi-billion-dollar industry and growing[2]. Its marketing and increased availability of products, including distribution of free samples, provision of free or low cost supplies to health facilities and financial or material inducements to health workers to promote designated products negatively affect breastfeeding[2].

The Newly Launched Sustainable Development Goals by 2030[41], a UN Initiative, tackle many issues faced by South Africa today such as poverty, hunger, child and maternal health, education, and reducing inequalities. Breastfeeding is clearly relevant to these goals. In South Africa, 41% of households have access to indwelling piped water[41]. The rest have little or no access to safe water supplies, making breastmilk substitute preparations a potential infectious risk for infants. With recent droughts and water restrictions, not only is the water potentially polluted, it is also scarce. More than 4000 L of water are estimated to be needed along the production pathway to produce just 1 kg of breastmilk-substitute powder[1]. By contrast, breastmilk is a natural, renewable food that is safe and environmentally sustainable, providing food security year round[1].

Two strategies have been reported to increase the rate of EBF: the BFHI, which was launched in South Africa in 1991 and the use of lay health workers such as community-based peer counsellors[18]. The latter is not yet established in South Africa. Breastfeeding offers a major healthcare benefit for all children without the need to wait for new vaccines, new drugs, or new technology, although all these must remain on the agenda to improve child health. Today's challenge, in the hospital services, is creating an enabling environment for breastfeeding of hospitalised infants.

Infant feeding practice during hospitalisation has not been formally assessed at RCCWMH, a tertiary care paediatric hospital. The purpose of this study is to determine breastfeeding rates in hospitalised patients, gain more insight into mothers feeding practices, to determine potential barriers to breastfeeding during hospitalisation to RCCWMH and to investigate the impact of hospitalisation itself on feeding practice.

Methodology:

Study Design: Prospective cross-sectional descriptive study of hospitalised infants less than six months of age to RCWMCH. Data will be collected over a period of 3-6months using a data collection sheet and questionnaire. Three interviews will take place: One close to or at the time of admission, one close to or at the time of discharge and a third telephonic interview approximately one-month post discharge.

Outcome:

1.Pre-hospitalisation
•To determine breastfeeding proportion of infants less than 6months of age hospitalised to Red Cross War Memorial Children's Hospital (RCWMCH), who breastfed exclusively
•Identify factors associated with exclusive breastfeeding
•Determine reasons for feeding choices and what alternatives are being used.
2.During admission
2a. Determine proportion who breastfed during admission
2b. Determine lodging arrangement during admission
2c. Open ended: In hospital barriers and experience of mothers
3.At follow up
•What proportion are breastfeeding approximately one month after discharge.

Subjects:

Primary caregivers and biological mothers of infants aged less than six months admitted to the general Paediatric wards (B1, B2) of RCWMCH.

Inclusion Criteria

- Primary caregivers and biological mothers of infants aged less than six months.
- Biological mothers younger than 18years of age, provided there is consent from a parent or legal guardian of the younger biological mother.
- Admission to the general Paediatric wards.

Exclusion criteria

- Primary caregivers and biological mothers of infants aged more than six months
- Primary caregivers and biological mothers of infants who do not own a phone or have access to a phone for telephonic communication

Data Collection:

Three Interviews (upon admission, discharge and at follow up) using a data collection sheet and questionnaire as referenced in Appendix B and C will be performed. Interviews upon

admission and discharge will be conducted away from the bedside in a private room within the ward. A third telephonic interview will be conducted within the RCWMCH premises approximately one month after discharge or before the infant reaches six months of age.

Definitions:

Infant Feeding Practices

Exclusive breastfeeding (EBF): breastmilk alone, not even water, except for ORS, syrups, vitamins and medicines

Mixed feeding: breastmilk in addition to other liquids or semi-solid foods. This is further divided into predominant and partial breastfeeding.

Formula Feeding (EFF): Formula milk in addition to other liquids and semi-solid foods. No breastmilk given.

2 Study Groups will include:

1a. Exclusive Breastfeeding

1b. Exclusive Breastfeeding and Mixed Feeding (Partial and Predominant Breastfeeding)

2. Formula Feeding

Investigators:

Medical Doctors and dieticians working in the general paediatric wards.

Statistical Analysis Methods:

A sample size of 75 per group would give an 82% power to detect a 30% difference in percentage of mothers who would stop breastfeeding after discharge between the two study groups. 150 sample size is a feasible amount in a 3month period and reflects number of infants less than 6months admitted to a specific ward.

Frequencies and proportions will be used to describe categorical variables. Chi squared testing will be used to evaluate statistically significant differences in baseline characteristics between breastfeeding and non-breastfeeding participants. Baseline characteristics include infant gestational age, birthweight, nutritional status (weight and length z-scores) and HIV status as well as maternal social class, HIV status, marital status, level of education, employment status, water source, sanitation and electricity availability.

Logistic regression will be used to assess factors associated with the different infant feeding practices.

Variables to be assessed in the regression analysis include infant nutritional status and HIV status, maternal social class, HIV status, marital status, level of education, employment status, water source, sanitation and electricity availability.

A p-value <0.05 will denote statistical significance.

Quantitative and qualitative data will be analysed using STATA Release 12.0 statistical software package (STATCorp, College Station, USA).

Outcomes:

Data will be presented at a national Paediatric conference and will be published in a peer reviewed article

Limitations:

Participants are not randomised. Selection bias based on participants more appropriate for the study.

Descriptive study carries less weight than a control trial. It is more open to confounding and bias.

The outcome of sample size will determine whether a statistically significant difference can be made. Recruitment of samples into the study is dependent on number of eligible samples hospitalised over time period of recruitment. This number varies during the year and may affect outcome of sample size. Samples lost to follow will affect sample size.

The interviewer bias and maternal recall bias.

Ethical considerations:

Data collection is anonymous and confidential. Patient privacy and confidentiality will be respected at all costs. Each patient will be allocated a research number and will therefore have their confidentiality protected. Data will be collected and stored in password protected computer folders and hard copies locked in an office to which only researchers have access. No additional tests or interventions will be performed on patients for the purpose of the study. Informed consent will be attained by mothers and translators will be used where language barriers exist. There is no direct benefit and no potential harm expected for participants. If barriers to breastfeeding can be identified and potentially addressed there may be benefits to the community. This study is in accordance with the International Declaration of Helsinki and other applicable ethical codes.

Budget:

Departmental funding of R5000 is required to cover data collection costs. Stationery, internet access and sundry costs will be covered by the Principal Investigator.

Timeline:

Protocol submission for Hospital Scientific Review by end of September

Ethics submission: By early in October of 2016

Data collection and analysis: Pending ethics approval, estimated to start by December

Intention to submit dissertation: In the Year 2018

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8.2 Appendix 2: HREC Approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

23 December 2016

HREC REF: 839/2016

Prof C Scott
Paediatric Rheumatology
Red Cross War Memorial Children's Hospital

Dear Prof Scott

PROJECT TITLE: FEEDING PRACTICES OF INFANTS HOSPITALISED TO A TERTIARY CHILDREN'S HOSPITAL IN THE WESTERN CAPE, SOUTH AFRICA (MMED CANDIDATE - DR M ALESIO)

Thank you for submitting your response to the queries raised by the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th December 2017.

- The HREC has the following suggestion for your information: Point 7 – the PI will exclude subjects who do not have a phone or access to a phone in the study. However, it may be possible to access these particular subjects for the third and final interview when they present for their follow up clinic appointment one month post discharge. This may help in maximising the sample size.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period. (Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the following MMed Candidate, Michelle Alisio, will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Yours sincerely

signature removed to avoid exposure online

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC REF 839/2016

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☐ Approved	Annual progress report	Approved until next renewal date	30/12/19
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	signature removed to avoid exposure online	Date Signed	28/11/2018

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol Information

Date (when submitting this form)	22/11/2018		
HREC REF Number	839/2016	Current Ethics Approval was granted until	30/12/2018
Protocol title	Determinants of infant feeding practices prior to, during and after hospitalisation to Red Cross War Memorial Children's Hospital.		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes ☒ No		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study			
Principal Investigator	Prof C. Scott		
Department / Office Internal Mail Address	Chris.scott@uct.ac.za		

HUMAN RESEARCH ETHICS COMMITTEE
27 NOV 2018
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

1.1 Does this protocol receive US Federal funding?	☐ Yes	☑ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval? **Note: Any annual approvals for Full Committee review MUST be submitted on the monthly HREC submission dates.** **(Please send electronic copy for full committee review to** hrec-enquiries@uct.ac.za)	☐ Yes	☑ No
If yes in 1.2 please complete **section 1.3 below for invoicing purposes**		
1.3 Annual Approval for full committee review	**- R 3420 (inclusive of vat)**	

For invoicing purposes: please provide:

Sponsor's name	
Contact person	
Address	
Telephone number	
Email Address:	

2. List of documentation for approval

3. Protocol status (tick ✓)

☐	Open to enrolment
☑	**Closed to enrolment (tick ✓)**
☐	**Research-related activities are ongoing**
☐	**Research-related activities are complete, long-term follow-up only**
☑	**Research-related activities are complete, data analysis only**
☐	**Main study is complete but sub-study research-related activities are ongoing**
☐	Study is closed → Please submit a Study Closure Form (FHS012)

4. Enrolment

Number of participants enrolled to date	119
Number of participants enrolled, since last HREC Progress report (continuing review)	21

(Note: Please complete the Closure form (FHS012) if the study is completed within the approval period)

Additional number of participants still required	0

5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	2

6. Cumulative summary of participants

Total number of participants who provided consent	119
Number of participants determined to be ineligible (i.e. after screening)	0
Number of participants currently active on the study	89
Number of participants completed study (without events leading to withdrawal)	92
Number of participants withdrawn at participants' request (i.e. changed their mind)	0
Number of participants withdrawn by PI due to toxicity or adverse events	0
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	0
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up	27
Unreachable on two telephonic contact details provided.	
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	3
Infants of enrolled mothers demised at or before the time of follow up.	

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:
The MMed candidate has completed data analysis and is currently making progress with the write up. The MMed candidate plans to submit before the end of December 2019

8. Protocol violations and exceptions (tick ✓ all that apply)

☑	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved

(Note: Please complete the Closure form (FHS019) if the study is completed within the approval period)

☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

☑	No prior amendments have been made since the original approval
☐	Prior amendments have been reported since the last review and have already been approved
☐	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).
Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.
No adverse events or unanticipated problems have been encountered. The Title of the study has been amended from "Feeding practices of infants hospitalised to a Tertiary Children's Hospital in Western Cape, South Africa to "Determinants of infant feeding practices prior to, during and after hospitalisation to Red Cross War Memorial Children's Hospital"

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g. in the case of abnormal or incidental clinical findings, distress or anxiety)?		
☐ Yes	☐ No	☑ Not applicable
If yes, please describe:		

11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. SAHPRA, FDA)?		
☐ Yes	☐ No	☑ Not applicable

11.2 Did a Data and Safety Monitoring Board publish a report?		
☐ Yes	☐ No	☑ Not applicable

11.3 If yes, please identify the agency and attach a summary of the findings.					
Agency Name		Report attached	☐ Yes	☐ No	☐ Not applicable
		DSMB report attached	☐ Yes	☐ No	☐ Not applicable

(Note: Please complete the Closure form (FHS013) if the study is completed within the approval period)

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?	
☐ Yes	☑ No
If yes, please explain:	

12. Level of risk (tick ✓)

12.1 In light of your experience of this research, please indicate whether the level of risk to participants has:	
☐	Increased
☐	Decreased
☑	Shown no change
If there has been a change, please explain:	

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.
N/A

13. Statement of conflict of interest

Has there been any change in the conflict of interest status of this protocol since the original approval? (tick ✓)	
☐ Yes	☑ No
If yes, please explain and if necessary attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form EHS013):	

14. Signature

My signature certifies that the above is complete and correct.			
Signature of PI	signature removed to avoid exposure online	Date	22 Nov 2018

8.3 Appendix 3: Consent and Assent Form

Consent Form: Participation in study of maternal feeding choices at Red Cross Children's Hospital.

Dear Mothers:

We are conducting a study on behalf of the University of Cape Town, to find out more details about the feeding choice you have made for your child (and why) and whether admission to hospital affects your feeding practice. We will be looking at 100-150 children less than six months of age admitted to the Red Cross Hospital wards.

To participate in this study, you will be asked to give consent for your child's feeding and medical information to be included. You will also be asked to give your general, medical and contact details to a doctor, nurse or dietician who will be working in the wards to do the research. The doctor, nurse or dietician will ask you to answer some basic questions regarding your feeding practice and reasons why you made this choice. We will not ask you to fill in any forms. We will not take any blood tests or x-rays. We will follow up the details of your feeding practice once your child has been discharged from the hospital via a telephonic conversation in your preferred language approximately one month after your discharge or before your infant reaches six months of age. The interview will be about 15 minutes and the telephone conversation about 5 minutes. Your child's medical information is totally confidential and will only be used for the purpose of this study and will not be shared with anyone who is not directly involved in the research. The ethics committee members or auditors may inspect some of the documentation. If you or your child is HIV positive this fact will be included in the study, but you and your child's identity will remain confidential. Your name and your child's name will not be used in the study. Please note that there will be no monetary compensation for your participation nor will there be cost to yourself.

Your child will receive the same optimal care, whether you decide to participate in the study, or not. You may withdraw from the study at any time. This will not affect your current treatment. You may contact the investigators or the HREC committee if you have concerns.

Potential benefits of this study are additional information on feeding practices and barriers to optimal feeding practices for children less than 6 months of age in the Western Cape. This may in the future be used to motivate for more educational and supportive in hospital and community based feeding practice resources. The study may be presented to national or international congresses, which would highlight the plight of your child and others.

Please feel free to ask us any questions if anything is unclear to you, before signing permission for your child to join the study.

Contacts

Principal Investigator: Prof C. Scott

084 580 5473 chris.scott@uct.ac.za

UCT Ethics Committee 021 406 6626/6492

This study is in accordance with the International Declaration of Helsinki and other applicable ethical codes. Thank you,

I, _____, hereby consent to participate in this

Study project, and for the medical information of my child

_____ , to be collected for this purpose.

Signed on _____/_____/2018 at

In the case of mothers under 18years of age

I, _____, (Parent or Legal Guardian of mother) hereby consent for the above signed mother
to participate in this Study project, and for the medical information of her child

_____ , to be collected for this purpose.

Signed on _____/_____/2018 at

Witness name _____

Witness designation_____ Signed on ___/_____/2018

8.4 Appendix 4: Questionnaires

#_____

months

Data Collection Sheet

Date of admission:

Date of interview:

Infant Research number and age at interview:

Mother/Primary Caregivers name:
……..……..

Captured Income Group (H0, H1…)……

Infants DOB/Hospital number:

Infants Gestation (weeks): Infants Birthweight(kg):

Infants place of Birth:
……

Infants gender: □M □F □I

Infants HIV status: □Exposed □unexposed □HIV infected □HIV uninfected

Diagnosis/Reason for admission: □Pneumonia
□Gastroenteritis
Other
……..

……

Nutritional Status Weight-for-age
Length-for-age

Weight-for-length

Appendix C:

Questionnaire

Maternal Demographic data

(Name and surname)
……
…….

Physical
Address……
……

Telephonic Contact details (at least x 2)
……

……
……

DOB/age:
……
……

HIV status □negative □positive □unknown

Other illness
……
……

First Language □iXhosa □Afrikaans □English

Other……
…….

Marital status □Married □Unmarried □Single Parent

Relationship with baby's father……

Education □Primary School □Gr8 – Gr9 □Gr10-12 □Tertiary

Employment status □Employed: Full time □Part time □Student □Unemployed

Water Source □Indwelling Piped □Outdwelling/Communal piped
□Not piped

Sanitation: □Communal toilet □bucket □ flush □flush toilet indwelling

Electricity: □Yes □No (alternative: paraffin…)……

A: PRE- ADMISSION PRACTICES – AT TIME OF ADMISSION/PRESENTATION TO THE WARD

Feeding Practice

1A. Exclusive breastfeeding □

1B. Mixed: Partial breastmilk introduction date: □AND liquids

AND/OR solids introduction date:

1C. Mixed: Predominant breastmilk introduction date: □AND liquids

AND/OR solids introduction date:

2. Formula Feeding/Never Breastfed introduction date: AND/OR solids □Bottle
□cup

B. Reason for feeding choice

1: Breastmilk is the best for the baby □

2: Formula milk is best for baby □

3: I was not producing enough breastmilk □

4: The baby did not want my breastmilk □

5: I am working/I had to go back to work □

6: Formula milk is expensive □

7: Advice or opinion of family member/friend □

8: Information from books/TV/magazines □

9: Advice from medical staff (doctor/nurse) □

10: I don't know □

11.Other……
……

C: DURING HOSPITALISATION- CLOSE TO OR AT TIME OF DISCHARGE

1. What feeds? □Breast/EBM □Formula □Mixed

2. How fed? □Breast □cup □bottle □NGT/OGT

3. Are you 'rooming in'? □Yes □No □I don't know

4. Are you using the lodger facility provided? □Yes □No □I don't know

5. Are you expressing? 5a. □Yes 5b. □No

5a. Share your experience of breast milk expression in hospital (i.e where/when/how often/comfort/support/attitudes in hospital……
……
……
……
……

5b. Why are you not expressing?
……
……
……
……

D: FOLLOW UP TELEPHONIC CONVERSATION

D: Discharge Date:

Date of Follow up telephonic conversation:

Infant age:

A: Feeding Practice

1A. Exclusive breastfeeding □

1B. Mixed: Partial breastmilk □AND liquids introduction date:

AND/OR solids introduction date:

1C. Mixed: Predominant breastmilk □AND liquids introduction date:

AND/OR solids introduction date:

2. Formula Feeding/Never breastfed □liquids

AND/OR solids introduction date:

E1. Reason for feeding choice

1: Breastmilk is the best for the baby □

2: Formula milk is best for baby □

3: I was not producing enough breastmilk □

4: The baby did not want my breastmilk □

5: I am working/I had to go back to work □

6: Formula milk is expensive □

7: Advice or opinion of family member/friend □

8: Information from books/TV/magazines □

9: Advice from medical staff (doctor/nurse) □

10: I don't know □

11:Other…….

E2. If feeding practice has changed:

What is the reason for change in feeding practice?

……
……

……
……

8.5 Appendix 5: Instructions to Authors of chosen Journal

Author Guidelines

The *SAMJ* has launched a new submission and tracking system. Authors will be required to register a profile on the Editorial Manager platform in order to submit a manuscript.

To submit a manuscript, please proceed to the *SAMJ* Editorial Manager website:

www.editorialmanager.com/samj

To access and submit an article already in production, please see the guidelines here.

Author Guidelines

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

SAMJ policies

- Types of articles considered by the SAMJ
- Article Processing Charges
- Authorship
- Conflict of interest
- Research ethics committee approval
- Clinical trials
- Protection of patient's rights to privacy
- Copyright notice
- Privacy statement
- Ethnic classification
- CPD

Manuscript preparation

- Preparing an article for anonymous review
- General article format/layout
- Preparation notes by article type
- Illustrations
- Tables
- References

From submission to acceptance

- Submission and peer-review

- Production process
- Changing contact details or authorship

Publication

- Online versus print
- Errata and retractions
- Indexing

SAMJ Policies

Type of articles considered by the SAMJ

The *SAMJ* will no longer limit the articles accepted to those that have 'general medical content', but is intending to capture the spectrum of medical and health sciences, grouped by relevance to the country's burdens of disease. This content will include research in the social sciences and economics that is relevant to the medical issues around our burden of disease. Please see 'A new vision for the *SAMJ* – and a call for papers' for a full discussion of the new directions for the *SAMJ*.

We accept the following types of articles:

Research
Reviews
Clinical trials
Editorials
In Practice (Previously Forum incl. Case Reports)
Correspondence
Obituaries
Book reviews
Ad hoc supplements e.g. guidelines, conference/congress abstracts, Festschrifts*

The following articles are by invitation only:

Guest editorial
Continuing Medical Education (CME)

*Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Publication Fees

All articles published in the *South African Medical Journa*l are open access and freely available online upon publication. This is made possible by applying a business model to offset the costs of peer review management, copyediting, design and production, by charging a publication fee of R5 250 (ex vat) for each research article published. The charge applies

only to **Research** articles submitted after 1 March 2017. The publication fee is standard and does not vary based on length, colour, figures, or other elements.

When submitting a Research article to the *SAMJ*, the submitting author must agree to pay the publication fee should the article be accepted for publication. The publicaiton fee is payable when your manuscript is editorially accepted and before production commences for publication. The submitting author will be notified that payment is due and given details on the available methods of payment. Prompt payment is advised; the article will not enter into production until payment is received.
Queries can be directed to claudian@hmpg.co.za.

Please refer to the section on 'Sponsored Supplements' regarding the publication of supplements, where a charge is applicable. Queries can be directed to dianes@hmpg.co.za or claudian@hmpg.co.za

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structuresto ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Clinical trials

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. All clinical trial reports must also contain a data sharing statement as per the recommendations of the ICMJE. Statements are to indicate:

- whether individual deidentified participant data will be shared;
- what data in particular will be shared; whether additional, related documents will be available;
- when the data will become available and for how long; by what access criteria data will be shared.

Please see the ICJME announcement for further details and illustrative examples of data sharing statements: ICMJE Data Sharing Statements for Clinical Trials

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The SAMJ therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Patient Consent

Information that would enable identification of individual patients should not be published in written descriptions, photographs, and pedigrees unless the information is essential for

scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAMJ*.

Copyright notice

Copyright remains in the Author's name. The work is licensed under a Creative Commons Attribution - Noncommercial Works License. Authors are required to complete and sign an Author Agreement form that outlines Author and Publisher rights and terms of publication. The **Author Agreement form** should be uploaded along with other submissions files and any submission will be considered incomplete without it.

Material submitted for publication in the *SAMJ* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. All research already published as 'Conference proceedings' needs to be substantially re-written, with a new title, a new abstract and new and important results to back up any study before it will be considered for a new publication. The *SAMJ* does not hold itself responsible for statements made by the authors.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

Privacy statement

The *SAMJ* is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered in the website or submission system will not be made available to third parties without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the *SAMJ* or its publisher HMPG on matters relating to the journal or associated publications. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a

detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAMJ is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, *SAMJ* also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).

- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

**NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'

- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

- Research
- Editorials
- CME
- In Practice and Case reports
- Reviews
- Clinical trials
- Correspondence

- Obituaries
- Book reviews
- Guidelines

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

CME (by invite only)

CME is intended to provide readers with practical, up-to-date information on medical and related matters. It is aimed at those who are not specialists in the field.

From January 2016, all CME articles will be printed in full in the *SAMJ*. Please try to adhere strictly to the guidelines on word count as we have a page limit for the print issue of the *SAMJ*. We reserve the right to place some tables and reference lists online if this is necessary for space.

In practice, this means that each CME topic usually covers two issues of the print issue of the *SAMJ*.

The guest editor, in consultation with the editor, is responsible for convening a team of authors, deciding on the subjects to be covered and for reviewing the manuscripts submitted. The suggestion is for 4 - 5 articles, although there is some room for flexibility contingent on discussions with the editor.

For queries about these guidelines please feel free to contact the CME editor, Dr Bridget Farham, by email (ugqirha@iafrica.com) or telephone (+27 (0)21 789 2331).

Review process

The guest editor reviews the articles and returns them to the CME editor for review and final approval.

Guest editorials

Guideline word limit: 1 000 words

- Include the guest editor's personal details (qualifications, positions, affiliation, e-mail address, and a short personal profile (50words)).
- If possible, include a photograph of the author(s) at high enough resolution for print. It is preferable to provide two guest editorials, one for each issue, so that the content of the articles in each issue is covered.

Articles

Guideline word limit: 2 000 - 3 000 words

- Each article requires an abstract of ±200 words.
- The editor reserves the right to shorten articles but will send a substantially shortened article back for author approval.

Personal details

Please supply: Your qualifications, position and affiliations and MP number (used for CPD points); Address, telephone number and fax number, and your e-mail address; and a short personal profile (50words)and a few words about your current fields of interest.

In Practice

Guideline word limit: 2 000 - 3 000words

This section includes articles that would previously have been accepted into the Forum section, and case reports.

In practice articles are those that draw attention to specific issues of clinical, economic or political interest regarding medicine and healthcare in southern Africa. They are assigned to a topic:

Case report
Clinical practice
Clinical alert
Issues in medicine
Issues in public health
Healthcare delivery
Consensus/Position statement
Medicine and the environment
Medicine and the law
Cochrane corner

An In Practice article should follow the following format – sub-headings are not necessary, but may be used for clarity:

- Author affiliations and qualifications: to be the same as for Research. Provide all authors' names and initials, qualifications and full affiliations, and corresponding author.
- Short abstract: does not need to be structured, but should capture the essential features of the article
- Introduction: the reason for the article and the issue being addressed
- Recent research, discussion, local policy around the issue – include your own research where appropriate
- All statements should be referenced and, if opinion only, this should be stated
- Discussion: how this article adds to the discussion around a particular topic
- If a clinical practice or policy point is at issue, this needs to be emphasised, using a box with highlights if appropriate.

Essentially In practice is an opportunity for a more discursive approach to topics of clinical, economic or political importance in southern African health systems. It is not an opportunity to put forward unsubstantiated opinions!

Case reports

The *SAMJ* has recently started to accept case reports. The cases must come from Africa, preferably southern Africa unless the condition is common to all African countries, and must be either a completely new description of a clinical condition or result (use Google!) or a case that highlights important practice or management issues.

Please use the following format for case reports:

- Title of case: do not include the words 'a case report' in the title
- Summary/abstract: up to 150 words summarising the case presentation and outcome
- Background: why is this case important and why did you write it up?
- Case presentation: presenting features, medical, social, family history as appropriate
- Case management: should be according to best practice, and if not, please explain why
- Investigations, if relevant: save space by simply saying 'normal' if, for example, renal function was completely normal, rather than listing normal results, highlight the abnormal – or indeed the normal if this is clinically significant
- Differential diagnosis, if relevant
- Treatment, if relevant
- Outcome and follow-up
- Discussion – a VERY BRIEF review of similar published cases
- Teaching points: 3 - 5 bullet points
- References: as per the *SAMJ* house style
- Tables and figures: keep to a minimum. Use clinical images where relevant – we need hi-res versions for print, and identifiable persons must have a consent form
- Patient consent: please include a statement about patient consent to a written case report. This should be uploaded as a supplementary file.

Clinical trials

Guideline word limit: 4000 words

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register.
The *SAMJ* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Review articles

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners.

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 500 words

Letters to the editor should relate either to a paper or article published by the SAMJ or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Book reviews

Guideline word limit: 400 words

Should be about 400 words and must be accompanied by the publication details of the book. Provide a hi-res image of the cover if possible (with permission from the copyright holder).

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Guidelines

Guidelines should always be discussed with the Editor prior to submission.

Because of the intensive review process required to ensure Guidelines are independent, evidence-based and free from commercial bias, they are usually published as a supplement to the *SAMJ*, the costs of which must be covered by sponsorship, advertising or payment by the guideline authors/association. We will provide a quote based on the expected length of the guideline and whether it is to appear online only, or in print, which must be accepted by the body putting the guidelines together before submitting the work to the SAMJ.

The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.

All guidelines should include a clear, transparent statement about all sources of funding and an explicit, clear statement of conflicts of interest of any of the participants in the guidelines about industry funding for lectures, research, conference participation etc.

All guidelines should be structured according to Agree II.

Please access this website before putting the guidelines together, download the Agree 11 instrument and use this to put the guidelines together.

All submitted guidelines will be sent to the local Agree II appraisal committee for review and must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed.

A structured abstract not exceeding 400 words (recommended sub-headings: *Background, Recommendations, Conclusion*) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2.etc.) and summarised in a Table of Contents.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.

- All illustrations (graphs, diagrams, charts, etc.) must be in PDF or jpeg form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:

Rather:

Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must* ***not*** *be used.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
  - On the Crossref homepage, paste the article title into the 'Metadata search' box.
  - Look for the correct, matching article in the list of results.
  - Click Actions > Cite
  - Alongside 'url =' copy the URL between { }.
  - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references

  • Government Gazettes:

  National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

  In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

  • Provincial Gazettes:

  Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

  • Acts:

  South Africa. National Health Act No. 61 of 2003.

  • Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

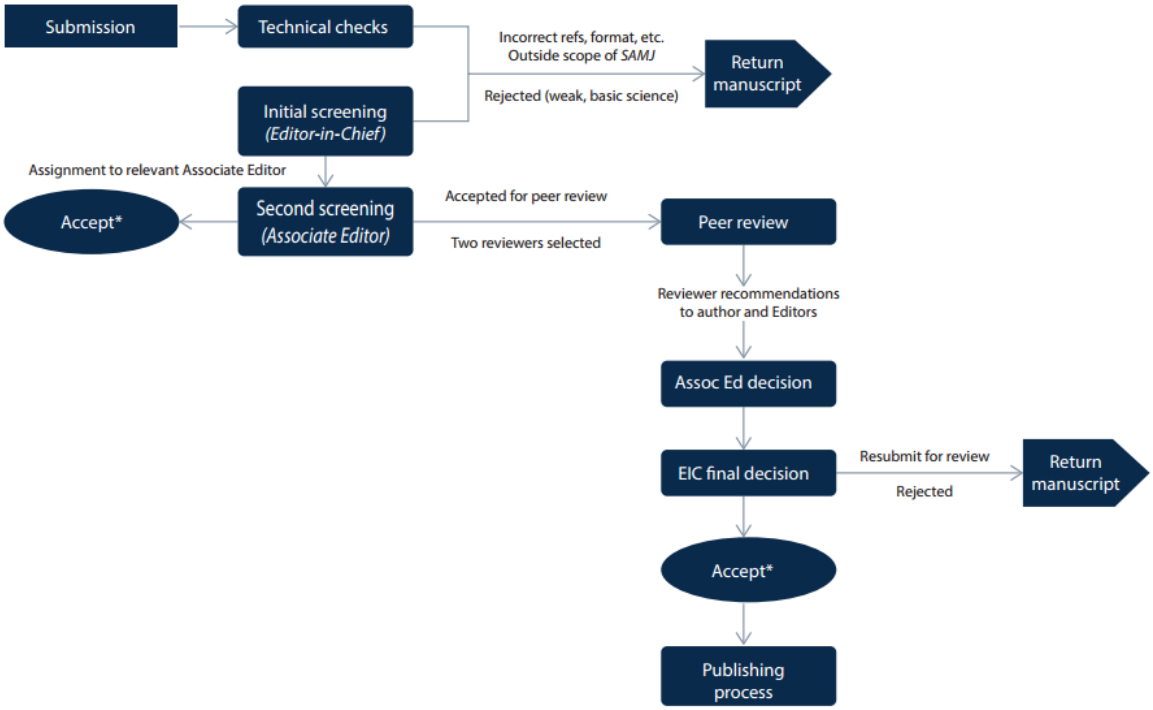
From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAMJ requirements.
- All submissions should be submitted via Editorial Manager
- The following are required for your submission to be complete:
  - Anonymous manuscript (unless otherwise stated)
  - **Author Agreement form**
  - Manuscript
  - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
- Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer-review process



*Manuscripts accepted at this point are limited to Editorials, Correspondence, Obituaries, Book reviews, Abstracts, CME
**Some minor revisions may be requested

Production process

The following process will follow:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Publication

Online v. print

The *SAMJ* is an online journal. The online version of the journal is the one that has the widest circulation, is indexed by bibliographic databases including PubMed and SciELO, and is accessible in academic libraries. A printed edition , containing material selected by the Editor is also published each month and distributed to the membership of the South African Medical Association.

Online

- The full text of all accepted articles is published in full online, open access.
- Citation information of each article is based on its online publication.
- You may want to make use of the advantages of online publication e.g. specify web links to other sources, images, data or even a short video.

Print

- Not all articles will be selected for print.
- An article may be selected for print in a different month from that in which it was published online.
- Research articles will appear *in abstract form only*, if selected for a print edition.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@hmpg.co.za,including the following details:

- Journal, volume and issue in which published
- Article title and authors
- Description of error and details of where it appears in the published article
- Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish anerratum in the next issue. The correction will be indexed, as PubMed has a function for linking errata back to the original article. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of HMPG. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.

Send an email to publishing@hmpg.co.za, including the following details:

- Journal, volume and issue to which article was submitted/in which article was published
- Article title and authors
- Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

The *SAMJ* has an impact factor of 1.5.

Published articles are covered by the following major indexing services. As such articles published in the *SAMJ* are immediately available to all users of these databases, guaranteed a global and African audience:

- Index Medicus (Medline/PubMed)
- ExcerptaMedica (EMBASE)
- Biological Abstracts (BIOSIS)
- Science Citation Index (SciSearch)
- Current Contents/Clinical Medicine
- Scopus
- AIM
- AJOL
- Crossref
- Sabinet
- Scielo

Sponsored supplements

Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2. The submission has not been previously published, nor is it before another journal for consideration. All research already published as ‘Conference proceedings’ needs to be substantially re-written, with a new title, a new abstract and new and important results to back up any study before it will be considered for a new publication.

3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
4. The manuscript is in Microsoft Word document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (PDF or jpeg). These must be submitted individually as 'supplementary files' (not solely embedded in the manuscript).
6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
7. Where possible, references are accompanied by a digital object identifier (DOI).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).

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Material submitted for publication in the *SAMJ* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement.

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8.6 Appendix 6: Turnitin Report

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ORIGINALITY REPORT

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SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	open.uct.ac.za Internet Source	2%

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Exclude bibliography	On		